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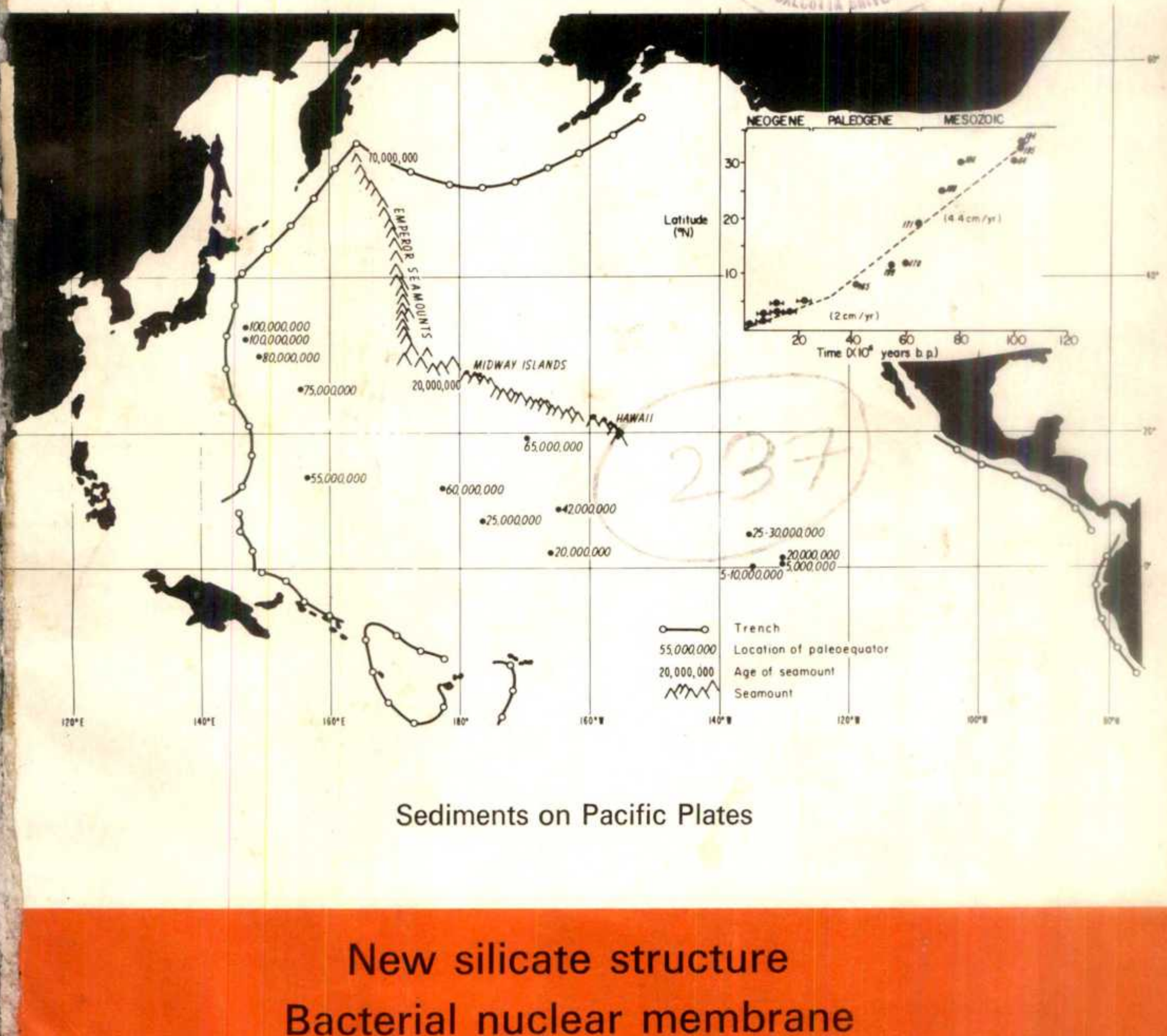

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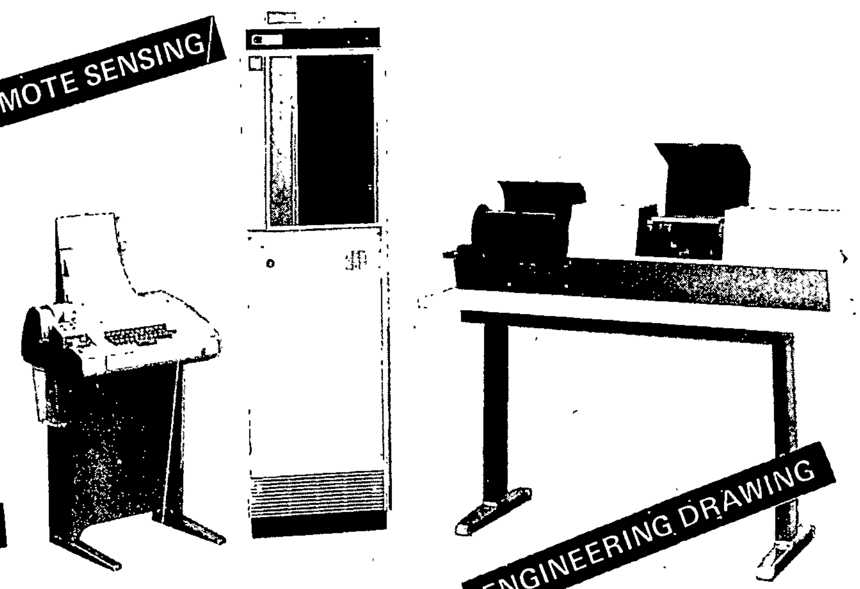

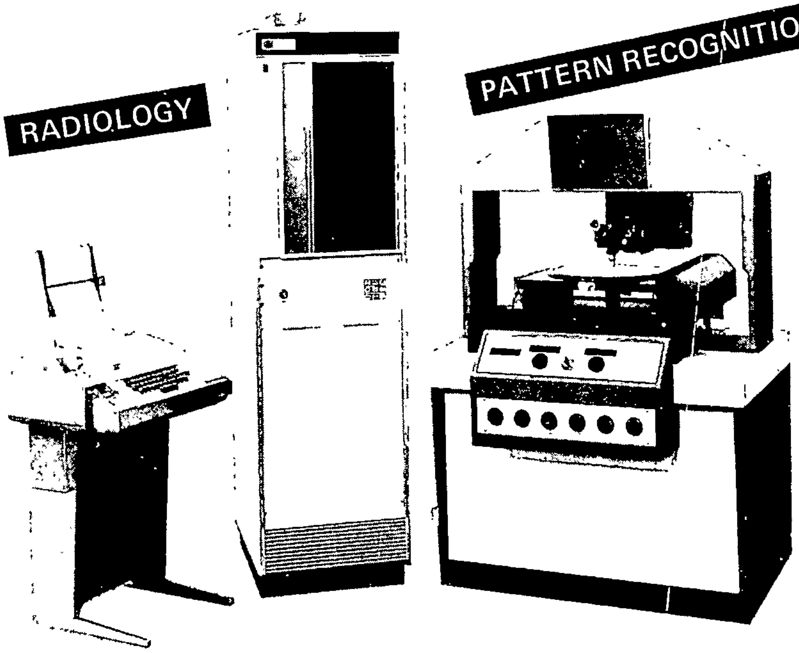

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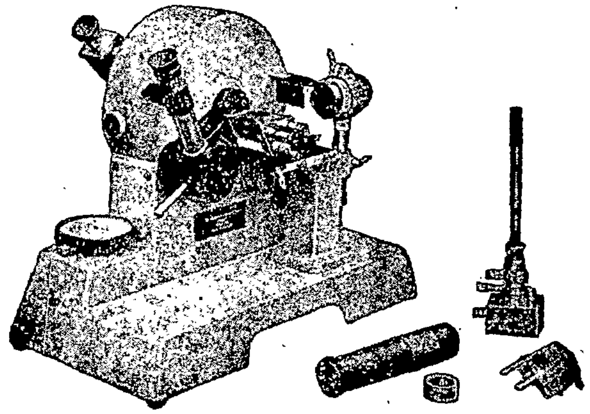

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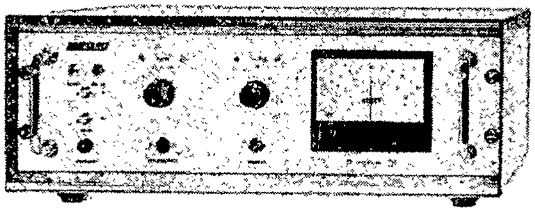

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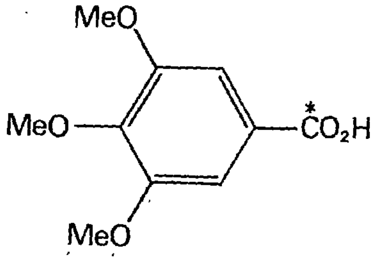

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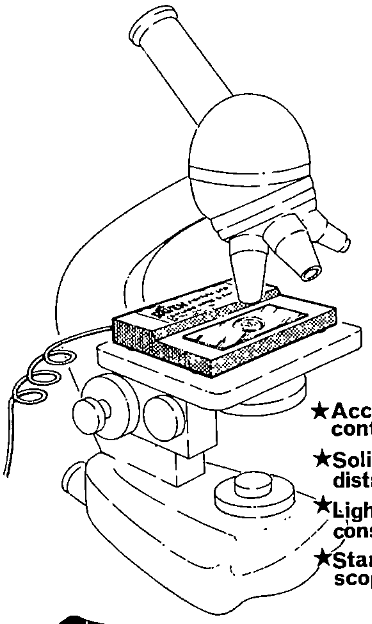

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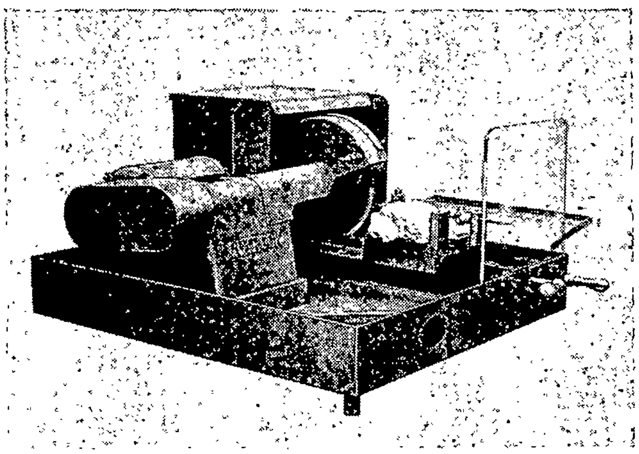

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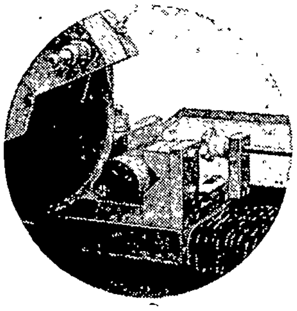

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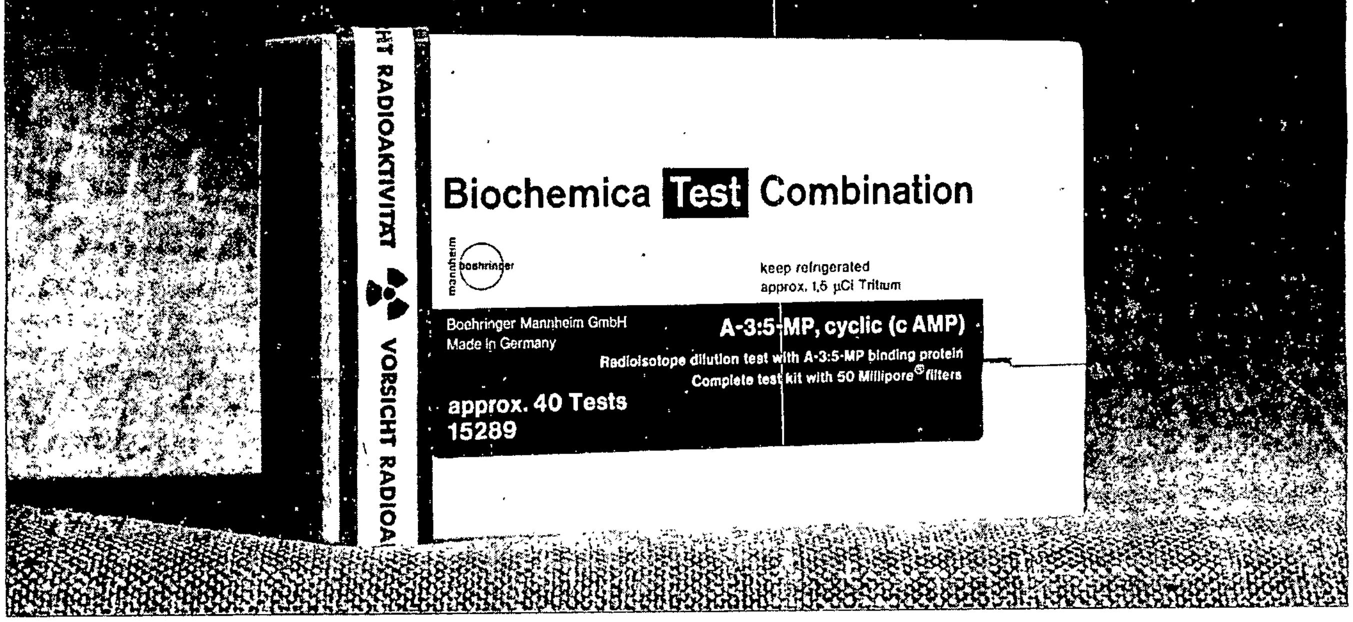

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NATURE Volume 241
JANUARY 5 1973

Consequences of the Bombing in Vietnam

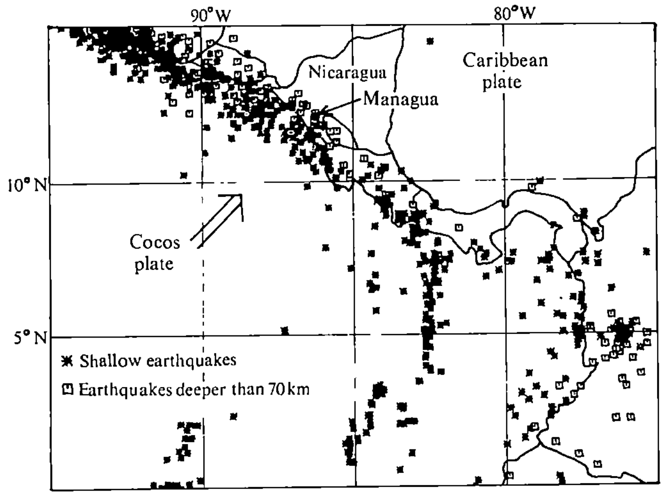
THE Vietnam war as such is no part of *Nature*'s parish (see *Nature*, **239**, 182 ; 1972) but the events of the past two weeks and the resumption by the United States of intensive bombing of North Vietnam above the 20th Parallel have raised issues which are bound to have an important influence, in the months ahead, in ways which the Administration in the United States has clearly either overlooked or deliberately ignored. The reasons why the bombing was resumed are, even now, by no means apparent. The United States Administration says that the breakdown of the peace negotiations in Paris a few weeks after President Nixon's successful re-election was a direct result of the intransigence of the North Vietnamese, but there is at least as much to be said for the view that the United States went back to Paris, after the election, with demands for a tightening of the draft agreement which could reasonably have been calculated to precipitate a breakdown. On the face of things, United States policy has been successful in that it has compelled a resumption of negotiations, with technical meetings in Paris this week and the arrival of Dr Henry Kissinger in Paris on Monday. By good luck, the Administration has been able to announce a resumption of the negotiations without having to acknowledge the force of the protests over Christmas that intensive bombing is, to say the least, an indecent substitute for diplomacy. What the United States has neglected, in its calculations of the consequences of the bombing, is that those governments which have protested will now be anxious to ensure that North Vietnam has a fair crack of the whip in Paris.

The coincidence of the bombing with the enlargement of the European Community is another part of the Administration's calculations which has either been done inaccurately or not done at all. Fortunately, the European Community has not become a kind of anti-American organization as might have been expected in the 1950s. Inevitably, however, especially now that it is a larger community than the United States itself, there is bound to be a re-examination of the extent to which Europe and the United States should coordinate their policies, not merely in defence but in economic affairs. And in the year ahead, there will be several opportunities for a redefinition of the transatlantic relationship. Where defence is concerned, the talks on Mutual Balanced Force Reductions scheduled for the spring and the European Security Conference in the summer will provide opportunities for European governments to work towards a lessened dependence on the United States. Although the United States itself will no doubt welcome an opportunity to reduce its military commitment to Europe, the Administration may well be discomfited by the tendency there will be to exclude it from other matters, some of them lying at the heart of the arrangements for the deployment of strategic power in Europe. But this year will also see another round of negotiations between Europe and the United States in Paris, the long awaited resumption in GATT of the Kennedy Round of tariff reductions, still incompletely implemented. There is now a serious danger that the bombing of North Vietnam will incline European governments against the further liberalization of trade across the Atlantic and with developing countries which has for several years been urgently necessary. It is to be hoped that in both these important areas, the governments of Europe will restrain themselves. Mr Nixon will not, after all, be President indefinitely, while the enlargement of the European Community and the diminution of the stature of the United States typified by the irrationality of the bombing over Christmas will make it easier for Europe to talk as an equal to the United States.

Another question raised by the bombing concerns the future of Dr Henry Kissinger, the architect of Mr Nixon's international policy in the past four years and the man chiefly responsible for the draft agreement on a peace settlement in Vietnam. Dr Kissinger is a distinguished scholar who deliberately took the risk of joining Mr Nixon's Administration in the hope, substantially justified by the experience of the past few years, that he would be able to exercise a liberalizing influence but no doubt conscious of the way in which many of his predecessors had been pilloried by academics for their association with the Administration's policy in Vietnam. There is now good reason to suspect that Dr Kissinger is not responsible for the bombing or even for the breakdown of the peace negotiations which preceded it. Indeed, there is everything to suggest that Dr Kissinger has been taken for a ride by the events of the past few weeks. In the circumstances, it is important that the academic community, and especially the students, in the United States should appreciate the difficulty and the delicacy of his position and that he should be given credit for his liberalizing influence in the past four years. But there are probably also good reasons why Dr Kissinger himself should now recognize that the time has come to return to Harvard, where his chair in international relations has been held vacant for the past four years but where a successor is likely to be appointed if he continues at the White House. Dr Kissinger's dilemma about the choice to make has been much publicized in recent weeks but the bombing should have helped make up his mind.

Nicaraguan Earthquake

THE awful lesson to be learnt from the earthquake which destroyed Managua, capital city of Nicaragua, on December 23, is that there may really be no economically feasible lesson in it at all. The earthquake killed upwards of 5,000 people and left Managua in ruins. The reason for it can be put all too precisely. The Cocos plate in the East Pacific is inexorably being thrust under Central America and the boundary between the Cocos and the Caribbean plate is along the western shore line of the Central American isthmus. The process of overriding the 50 km thick Cocos plate and essentially of swallowing it at a rate of several centimetres a year produces a belt of high seismicity along this whole shoreline. Several hundred detectable earthquakes occur each year on this 2,500 kilometre convergence zone. The majority of them are underwater, but a significant fraction occur on land. The Managua earthquake was a magnitude 6 event—a factor of a hundred smaller in fault length than the magnitude 8 events such as San Francisco 1906 and Alaska 1964. The destruction wreaked by smaller events depends on close proximity (perhaps to within a few kilometres) of civilization. Thus this earthquake will go down with Agadir 1960 and Skopje 1963 as events of magnitude 6 which occurred near centres of population and killed thousands.



Seismicity from 1961–9. Map is produced by U.S. Department of Commerce, National Earthquake Information Center.

Managua does not lack a history of seismic damage. In 1926, half the city was destroyed by an earthquake. In 1955 and 1964, it suffered further damage. There is not a shred of evidence to suggest that the most recent earthquake will do more than temporarily relieve built-up stresses. Past seismicity is rather a good guide to where future earthquakes can be expected. And in this present state of seismological understanding there seems no way of capitalizing on information gained during this earthquake without enormous expense. The four possible courses of action are to stop earthquakes, to predict them, to remove towns from earthquake zones and to enforce rigid building codes. The first course would involve either stopping the Earth's convective motion or lubricating all known faults. The second course looks slightly more plausible on the basis of recent Russian results—provided that the technology is available, a high false alarm rate is acceptable and people have time to move. The third course is somewhat more plausible, although in a country like Nicaragua this would involve permanently evacuating the whole western coastal areas—in California presumably the only utterly safe thing to do would be to evacuate San Francisco and Los Angeles. The fourth course has met with some signal success in the United States. The San Fernando earthquake (1971) provided striking evidence of the efficacy of building codes, but there is, of course, an urgent need for similar codes for highway bridges, transformers and the interior features of buildings. Whether even a rudimentary code could be enforced at any reasonable price in Nicaragua or other countries in this region is doubtful, to say the least.

Decisions on whether a government should attempt an earthquake protection programme are clearly as much political as scientific. As yet, however, no country seems to put as much investment into protecting itself from natural disasters as from outside invaders. Thus we shall probably see an expedient solution to the Managuan problem in that the zone in which the damage was greatest will be avoided in rebuilding. A similar policy was followed at Agadir. There is no scientific justification at all for this. No one knows whether stress has been relieved in the surrounding regions. Besides which, many of the destructive earthquakes at Nicaragua are deep (that in 1926 was at a depth of 150 km). Moving the site of a city by a few kilometres can do nothing to reduce damage from earthquakes like these.

It goes without saying that the inevitability of earthquake damage in the now well recognized seismic regions makes a mockery of the attempts to organize emergency relief for damaged cities such as Managua. The surprise with which well-meaning governments repeatedly find themselves making allocations of inadequate funds for purchases of food and medical supplies is all too reminiscent of the astonishment with which the British government reacts whenever there is a heavy fall of snow in Scotland. The truth is that the world must learn somehow to live with or to survive as best it can the natural disasters which, in the nature of things, must repeatedly recur in vulnerable places. And it is now clear that only the United Nations is sufficiently well placed to organize the kind of emergency aid that will be needed for as long as cities such as Managua are vulnerable to earthquakes—and cities such as Calcutta to typhoons. Much has been heard, in recent years, of schemes like this but nothing so far has happened.

Poor Substitute for Annan

One of the last acts of the last Labour government in 1970 was to set up a committee to inquire into the future of broadcasting in Britain after 1976. The then Minister of Posts and Telecommunications, Mr John Stonehouse, when announcing the formation of the committee, to be headed by Lord Annan, spoke of the "breathtaking technological environment" in communications which had come to exist. The scope of the Annan Committee was therefore to be broader than of those in the past: Pilkington in 1960, Beveridge in 1949, and Ullswater in 1936. Technical changes might even, he conjectured, allow the quasi-monopoly of the broadcasting organizations to disappear.

One of the first acts of the Conservative government was to disband the Annan Committee. Not that Mr Christopher Chataway disagreed with the enthusiasm of his predecessor for the new technology (although he never risked being teased for his effusiveness). But he did not think that it was the best way to approach the decisions of 1976, when the various legal instruments authorizing the British Broadcasting Corporation, the Independent Broadcasting Authority and the various private commercial companies selling wired (or cable) television services expire. At the time Mr Chataway saw two obstacles to another Pilkington. First, British broadcasting was falling into a pattern of ten-year cycles punctuated by full-scale inquiries; during the last years of the cycles nobody wanted to decide anything pending the outcome of the inquiry. Second, the technological possibilities were now genuinely novel. There were satellites, multi-channelled cable television and video-cassettes. The best thing, so Mr Chataway argued, was to revive the ministry's Television Advisory Committee, let it spend a year delineating the new alternatives on a purely technical basis and then the government could weigh the political and social advantages of using any of them to modify or reform present broadcasting arrangements. The TAC, under the chairmanship of Sir Robert Cockburn, was to report by January 1972, in order that there would be sufficient time for study before legislation needed to be drawn up.

Things have not turned out that way. The TAC's report has just emerged, a year late. It is provincial, conservative and misleading. Far from describing any opportunities for change, breathtaking or not, it spends most of 21 pages hashing over the BBC's and IBA's technical problems in extending UHF 625-line television coverage to as large an audience as could receive the old 405-line VHF signals now being abandoned. It takes as a basis the Pilkington Report's recommendations that six channels of national television are still the country's objective, and in fact could almost have been written by BBC engineers 12 years ago.

Here briefly are the committee's conclusions on the new communications technology. 1. A fourth television channel, using UHF and a 625-line standard, is immediately available. 2. About 1985, two extra television channels could be added by using the two broadcast bands on VHF which will be vacated when the current 405-line black-and-white transmissions of BBC-1 and ITV are ended and the transition now in progress to the UHF 625-line standard is completed. 3. Television broadcasting direct from satellites cannot be expected until the 1980s and could provide four programmes of national or near-national coverage. 4. Wired television on a national scale costs too much to be considered in the 1976 decisions. 5. Wired television can, however, help distribution of programmes in remote and rural regions and it could be used to provide local television programmes. 6. Video-cassettes, because of lack of standardization, are unlikely to come into domestic use in the period likely to be affected by the next franchise period (assumed to be twelve years).

In other words, the much touted communications technological revolution is a long way off and expensive to boot. Hence no need to change. Such conclusions should not be surprising from a committee constituted as the TAC has been, heavy with representatives of the *status quo*—the BBC, the IBA and the Post Office are all threatened by the new technology, particularly by cable television. It is no accident that nowhere in its report does the TAC mention the primary advantage of wired television, that it offers a solution to the basic problem of British broadcasting—a shortage of frequencies to accommodate the varieties of radio and television programmes that people would like to receive.

The recommendation that the VHF should be "re-engineered" in 1985 for two extra channels of television is an idea that has been kicking around the ministry for years, certainly since Pilkington. Yet nowhere does the TAC report mention the fact that the VHF is the most desirable part of the spectrum for land mobile communications, a fast-growing service in the United States and one which is sorely lacking in the United Kingdom. Nowhere does the report mention the possibility of using the vacated VHF for more radio, nor does it mention the growing demand for the use of radio and television for specialized audiences. The Open University, for example, is not mentioned in the report. Yet the Open University has illustrated the need for extra channels at peak viewing and listening hours. The university's students want to tune in just when the BBC's biggest popular audiences also want to receive their programmes. The Open University could well expand by using radio instead of television—especially if rumours are true that those students of the Open University who are doing best are those who live in areas where BBC-2 television is unobtainable.

The TAC report shows the fallacy of believing that there is such a thing as pure technology. It protects the interests of those who wrote it, without bringing together the kind of plain factual information that politicians and the public should have before facing 1976. One would never believe, if this report were a guide to communications technology, that cable television systems can carry signals in two directions, that they are expected, in the United States, soon to distribute the mail and facsimiles of documents in large cities. Nor would one know that direct broadcasting from satellites was real enough for India to plan to use it to give educational television to 5,000 villages in a few years' time. Nor that there is an alternative to Britain owning its own satellite or helping to build a European one: Latin America is receiving a constant flow of television from Spain and Portugal because a share of Intelsat's satellites has been rented, and Brazil intends to do the same soon for a domestic educational broadcast network. Nor that in France the state broadcasting monopoly and the PTT are concerned enough about the potential of cable television to have set up a joint enterprise to study it.

What was the TAC's job if not to put such information on the state of the technology before the decision-makers now? Members of Parliament or executives of the BBC cannot be expected to pore over the fine print in *Aviation Week*. But one unforeseen benefit of this timid, self-protecting report could be to diminish the importance of 1976. The report would have it that no great technological changes need alter the *status quo*. The truth is the opposite—that the changes are tremendous and that the pressure of, say, international satellites plus multi-channelled local wired distribution will be felt all over Europe by 1980. But 1976 is too soon to make profound changes in the present broadcasting systems, and if this report has bought time it is worth something. What should be done in 1976, in fact, is to agree on a temporary continuation of the *status quo* but to permit much more experiment outside the two broadcasting authorities. The local television experiments in Greenwich, Bristol and several other cities are a good thing. Satellite broadcasts should be tried; so should two-way cable systems (that installed at Bletchley is supposed to contain two-way capacity). So should public-access television. Those are political decisions, to be sure, and if more technical advice is needed before they can be taken, it should be sought from objective consultants, not from the vested interests who stand to lose most from change.

Science Overlooked

THE British government has been commendably resolute in its efforts, in the past few months, to make Britain a part of Europe again, but its arrangements for celebrating the occasion have been curiously haphazard. Altogether, something like £300,000 has been spent on what is somewhat euphemistically called a "Fanfare for Europe"—a programme of concerts, theatrical performances and exhibitions devised by a committee with Lord Goodman as chairman. It may be that Lord Goodman is the best of all Pooh-Bahs, but he seems to have fumbled badly. Although the objective seems to have been to draw attention to the cultural relationship between Britain and the mainland which has existed for the past several centuries and which has now, with luck, become stronger, the programme which has been devised (*Fanfare for Europe,* Arrow Books, £0.70) is almost entirely innocent of attempts to demonstrate that many of the most important links between Britain and the rest of Europe have their roots in science. The nearest that the official programme comes to a recognition of the importance of science is an exhibition of ancient boats, recently dug up, at the National Maritime Museum. For the rest, there is not merely plenty of good music but a competition in karate between Britain and France, a basketball tournament, a volleyball match between teenage teams from Scotland and Belgium, an exhibition of stamps and other sporting contests, in fencing and weight-lifting, all too familiar as a means of disrupting international relations, not of cementing them. It is true that Lord Goodman's committee may not be the one solely responsible for the entire neglect of science in this programme of events—Lord Mancroft, a famous after dinner speaker, had a parallel committee responsible for what are called "other events", the fencing and the weight-lifting. The most charitable explanation is that science fell between the two committees; the most likely is that it was forgotten.

What might the committees have done? Especially with the Copernicus quincentenary, even the good Lords Goodman and Mancroft might have been moved to mark the reunification of Britain with Europe by recalling the time when the foundations of modern science were constructed by Tycho, Keppler, Copernicus, Galileo and ultimately Newton. They might also have remembered the several periods in European history when the scientific community has been more strongly welded together than any other community, with the possible exception of the Catholic Church. Did Davy and Faraday go gallivanting about France during the Napoleonic Wars for nothing? And is there not at least something favourable to be said for the way in which there has grown up several strong scientific institutions in Europe, of which CERN is the most conspicuous example (and several bad ones as well), whose work deserves some recognition in what is supposed to be a celebration of cultural links.

The neglect of science in *Fanfare for Europe* is not merely a debating point. Given the Prime Minister's devotion to music, it may be held that music, even pop music, is what the occasion called for. And it is certainly true that literature is also dealt with skimpily in the Fanfare, as are the humanities. But the overriding issue is whether it is in any sense proper that when people, even Lords Goodman and Mancroft, think of culture, they should think first of those kinds of culture which can be most easily exhibited by means of a few telephone calls to impresarios, theatrical agents and museums. The truth is that the contribution of European scholarship in general and European science in particular to the fabric of modern life is as much cultural as practical and is on all counts indispensable. To forget this is often forgiven but is unforgivable.

In practical terms, what *Fanfare for Europe* might have included is an exhibition to show how the foundations for modern science were laid in Western Europe, how the Cartesians raised the banner of applied mathematics, how people such as Gauss and Huyghens were able to conjure up insight out of thin air and how the experimentalists such as Volta, Lavoisier, Black and Faraday (to mention only a few) created the sense which now runs through science that a theory is above all a concept to be tested. And if by any chance the organizing committee had run short of interesting topics with which to deal, there would always have been the half century which began with Darwin and Maxwell and which, by the first decade of this century, had reconstructed modern science and had drawn the whole of Europe into the enterprise. Even to imply by default that these great happenings are not cultural is to deny what everybody knows—that the way in which all people regard the world they live in has been transformed as much by scientific discovery as by any other intellectual process with its roots in the Renaissance. To be sure, it is often harder to make all this come alive than to remind people that Beethoven was a genius, but that is no excuse for not trying. The simple truth, however, is that between them Lords Goodman and Mancroft have done a shallow job. In many ways, the Prime Minister might have been better advised to have substituted for *Fanfare for Europe* a public holiday on January 1, widely kept as such in any case.

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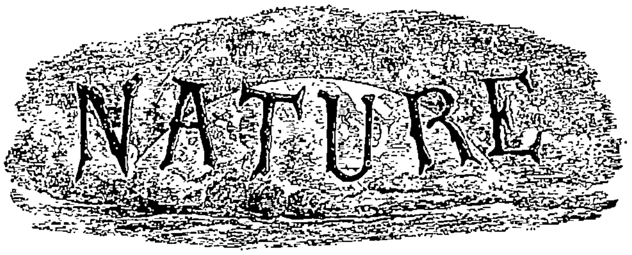
100 Years Ago



NOTES

WE believe that a reply has been received from the Government on the subject of the Arctic Expedition, which goes far to justify all that was said in our leader last week on the subject; for although the Government does not refuse absolutely to comply with the wishes of the deputation, all action will, unless strenuous efforts are made, be postponed for a year. We repeat that the deputation did not represent Science so broadly as it ought to have been represented; and we add, that if the Government thought so, it was, in our opinion, perfectly justified in refusing the demands made upon the national purse. To a certain extent, what happened in the case of the Eclipse Expedition of 1870 has been now repeated. Our readers will recollect that on that occasion the mere personal application of the Astronomer Royal was at once very properly refused, while a proper representation by the leading Societies was at once as promptly acceded to.

From Nature, 7, 188 and 189, *January* 9, 1873.

OLD WORLD

Too Much Freeze

MORALE among scientists working in government laboratories is lower than it has ever been, according to the Institution of Professional Civil Servants. Scientists are disenchanted according to Mr William McCall, general secretary of the IPCS, because of the government's constant refusal to set up an independent committee to determine the criteria by which pay for scientists within the civil service should be determined.

The government claims that pay research, by which pay of scientists within the government is compared with the pay of scientists working in industry and non-government establishments, is the most appropriate way of determining pay scales for its scientists. The IPCS, on the other hand, following many years of disagreement with the principle of pay research for scientists which culminated in the summer of 1971 with mass meetings and an independent tribunal, has vowed that there will never be another pay research exercise for government scientists.

A way out of this impasse was first put forward by the IPCS in August 1972, when it suggested the setting up of an independent committee. As yet, the government has not acceded to the request, with the result that both the IPCS and its members are becoming impatient. The IPCS has said that it will abide by the decisions of the independent committee even though it may recommend that pay research is indeed the best way.

At present, the science category is bottom of the pay league within the civil service. In 1969 the Administration, Science and what is now known as the Professional and Technology categories, had comparable maximum salaries for the Administrative Principal, Principal Scientific Officer and Principal Professional and Technology Officer grades, but since then the PSO has been left sadly behind. The Administrative Principal now commands a salary of £4,708 at the top of the scale, the Principal PTO £4,760, while the PSO has a maximum of £4,387.

The decision on whether or not to set up the committee has been affected by the government's pay freeze, and it is understood that the extended delay in making a decision is due to differences in opinion between government departments. The IPCS maintains that there is no conflict between the proposal to set up the committee and the government's pay freeze, for the committee is to be concerned with criteria for determining pay, not with awarding increases.

The Civil Service Department said this week that it was "actively considering" the IPCS's request. Mr William McCall also said this week that the institution would have to consider the possibility of action—even stronger than that taken in 1971—if the government did not respond satisfactorily.

ROYAL SOCIETY

Research in Schools

THE Royal Society supported a hundred research projects in schools last year through its Scientific Research in Schools Committee. The scheme—which has been running since 1957—exists to enable school science teachers to undertake original research; it is financed by the Atomic Energy Authority and six companies who provide about £3,000 a year.

The committee receives about thirty applications a year from teachers and approves about twenty-five of them, providing applicants with items of equipment that their schools cannot supply. Although the grants are usually small—normally less than £100—the committee has been known to give grants of up to £600 to buy items such as a spectrophotometer. The object of the scheme is to encourage bright science graduates to enter teaching by providing them with the facilities for research if they have the time and the necessary skills. When a teacher applies for a grant he is sounded out by an adviser from his local university, who is on hand to help throughout the project.

Mr N. A. W. Le Grand, the secretary of the committee, points out that the Royal Society is anxious to support as wide a spectrum of projects as possible; current projects range from studies of pollution in the Tees Bay area to the measurement of the stability of metalamine complexes to work on radio astronomy and colour blindness. The Royal Society encourages the recipients to publish their results, and last year thirteen papers appeared in the literature as projects were completed.

Each grant is made personally to the teacher and not to his school, but the Royal Society examines the facilities of the school and the support it is likely to give the teacher before it makes a grant. The society does not automatically turn down applications from teachers who cannot involve any of their pupils in their work, but such involvement is encouraged and one effect of the scheme has been to interest pupils in research, leading them to read science at university.

The time scale of the projects varies enormously. One on corrosion has been running for ten years, some involve seasonal studies for a number of years but other are relatively short lived. Since publicizing the scheme more widely two years ago (thousands of leaflets were mailed to schools and colleges of education all over the country), the Royal Society has been particularly eager to support practical research projects rather than pure research, which it feels is usually the province of the universities. The results have included a redesign of the scrubbing brush, which has been taken up commercially, a receiving station to pick up pictures from weather satellites, and a pram alarm that could prevent baby snatching. But the society is also supporting many more basic projects.

METEOROLOGY

Watching the Sun

from our Soviet Correspondent

AN unofficial "weather prophet" from Gornaya Shoriya in the Soviet far east has won official recognition for his theories of long range forecasting that solar activity influences weather not only through variations in heat flux but also through other forms of radiation and that sun spot activity and variations in the solar wind should also be taken into account in long range forecasting.

Anatolii V. D'yakov, who mans the tiny meteorological station of Gornaya Shoriya assisted only by his wife, has for several years been issuing unofficial forecasts, particularly to the agricultural planners of the Virgin Lands. Although the recipients of these forecasts found them more than satisfactory ("Do we use them? We are guided by them!", commented Academician A. I. Baraev of the All-Union Institute of Agricultural Sciences), the director of the Hydrometeorological Centre, Professor B. A. Bugaev, considered them little more than "charlatanism".

The success of D'yakov's three month forecasts, however, attracted considerable press coverage, first in local Siberian journals and finally (September 27, 1972) in *Pravda*. At the end of October D'yakov was invited to address an All-Union conference on the problem of the interaction of the Sun and the lower atmosphere. This conference resolved *inter alia* to implement a research programme on the effect of solar activity on the weather, stressing that "the rational approach to long range weather forecasting should take into account the whole totality of the perturbing factors and their variation in time". A working council to consider the problem of solar effects has been set up to work in collaboration with the Principal Geophysical Observatory (on long range forecasting) and the Hydrometeorological Centre (on short range forecasting). As part of the programme D'yakov is to prepare his own long range forecasts for 1973–74 "by way of experiment" and to submit them to the Hydrometeorological Service "for appraisal". The working council also consider it "suitable" to transfer the Gornaya Shoriya "helio-meteorological station" to the jurisdiction of the Soviet Academy of Sciences or the Hydrometeorological Service.

REACTORS

European Neutrons

BRITAIN has bought a one-third share in the Franco–German high flux reactor at Grenoble for £10 million. British participation in the reactor project comes after negotiations conducted by the Science Research Council on behalf of the government, which has provided the SRC with the necessary funds to participate in the scheme. The SRC will spend almost £2 million a year in running expenses and a further £1 million a year for ten years in capital.

The agreement, which took effect on January 1, provides that the SRC will have one-third representation on the Steering Committee, the Scientific Council and the Audit Board of the Institut Max von Laue–Paul Langevin (ILL) where the reactor is situated, and provides that the director of the ILL will be alternately German or British. British scientists will have a fair share of scientific posts at the institute, and preference will be given to British companies in the placing of some of the contracts for future work.

The SRC began negotiations with the French and Germans in August last year, following a decision by the British government not to build a high flux reactor in Britain (see *Nature*, **239**, 60; 1972). The SRC Committee for Neutron Beam Research originally decided that Britain would benefit more by building its own reactor at a cost of £22 million than by joining France and Germany at Grenoble, but the government turned down the council's request for funds. The cost of the new arrangements will be only half that of a solely British reactor, but British scientists will have to be content with only one-third of the experimental time that they would otherwise have had.

The United Kingdom Atomic Energy Authority said this week that some of its long term neutron beam experiments will be transferred to Grenoble, possibly this month, but a spokesman pointed out that the Grenoble reactor—which went critical in August last year—does not have the irradiation facilities envisaged in the proposals for the British reactor. "There is therefore a growing need to find alternative irradiation facilities."

One of the alternatives could be the construction of another high flux reactor by the three countries, but this time in Britain as provided for by a clause in the SRC's agreement.

COMPUTERS

Watching a Watchdog

THE Civil Service Department has created a Computer Agency Council to advise on the development of government data processing, and "to define areas where action is required by the Central Computer Agency . . . to promote the efficient application of processing systems in government departments".

This is the latest step in a rationalization of the previously complex machinery involved in the purchase of computers for use in government departments. Until the Central Computer Agency was set up in April last year, a few months after a recommendation by the Select Committee on Science and Technology (see *Nature*, **236**, 254; 1972), the responsibility for this was shared between the Civil Service Department, the Department of Trade and Industry and the Stationery Office. But now some 600 civil servants, under the direction of Mr Stephen Spain, carry out the same functions within the Civil Service Department itself. (Of these, about 300 work at the agency's Central Computer Bureau at Norwich, which provides a computing service for those government departments that require it, about twenty-five are responsible for policy planning, and the remainder are concerned with purchasing, contracts and so on.)

At the end of 1971, 213 computers were installed within government departments—45 per cent of them for scientific purposes—and the present rate of government expenditure on computing facilities is about £35 million a year.

The new Computer Agency Council will initially have twelve members and the chairman will be Mr Kenneth Baker, Parliamentary Secretary at the Civil Service Department. Seven of the members, including Mr Spain, represent government departments, and the other five are drawn from non-government bodies which have experience of the use of computers. Among them are Sir Brian Flowers, chairman of the Science Research Council, and Mr C. P. Williamson of British Petroleum. The Civil Service Department says that, through the council, it hopes to be able to benefit more fully from expertise in the private sector. The council is expected to have its first meeting later this month.

New Year Honours List

IN the Honours List announced this week, D. A. K. Black, Professor of Medicine at the University of Manchester; Professor Theodore Crawford, Director of Pathological Services at St George's Hospital and Medical School; Eric Eastwood, Director of Research, General Electric Company Ltd; and F. G. Young, Professor of Biochemistry at the University of Cambridge, were made Knights Bachelor. Professor Herman Bondi, Chief Scientific Adviser to the Ministry of Defence, and Professor Claus Moser, director, Central Statistical Office, Cabinet Office, were made Knights Commander of the British Empire; and Miss Kathleen Kenyon a Dame Commander of the British Empire.

SOVIET SCIENCE

Interkosmos Programme

from our Soviet Correspondent

THE launch on December 1 of the latest COMECON satellite, Interkosmos-8, carrying ionosphere research experiments provided by Bulgaria, East Germany, Czechoslovakia and the Soviet Union, was the occasion for a special interview in *Pravda* (December 2, 1972) with Academician Boris Petrov of the Soviet Academy of Sciences on the whole purpose and future of Interkosmos. Academician Petrov is a leading figure in both the Soviet and the Interkosmos space programmes.

According to Academician Petrov, the chief aim of the Interkosmos programme is to gather information on the solar and galactic flux, cosmic rays and micrometeorites. The investigations have, so far, covered the active regions of the ultraviolet and X-spectra (Interkosmos 1, 4, 7), low-energy cosmic rays (Interkosmos 3 and 5), and ionosphere and magnetosphere processes.

Interkosmos-8 is continuing the ionosphere investigations of Interkosmos-2, but in contrast to its predecessor it is investigating the magnetic poles and the aurora. It is hoped that this will enable the connexion between geophysical and geomagnetic processes to be traced more clearly.

NEW WORLD

AAAS at the Crossroads

from our Washington Correspondent

ALTHOUGH eight people were arrested during a clash with police, the 139th annual meeting of the American Association for the Advancement of Science, held in Washington last week, was one of the quietest for several years. Members of a radical group of scientists known as SESPA (Scientists and Engineers for Social and Political Action), which campaigns under the slogan "Science for the People" and which has added a touch of colour, if not of harmony, to the previous three AAAS meetings, were notably thin on the ground—there were no tomatoes thrown at politicians or stabbings with knitting needles—events which have grabbed the headlines at past AAAS gatherings.

Instead, participants in the meeting were confronted with an array of lectures and symposia dealing with issues ranging from pollution control, economic growth and social responsibility to esoteric discussions of research results. Like the annual meetings of the British Association, the AAAS gatherings have become notably more political in the past few years—due in part to the proddings of SESPA—and they are increasingly running up against the knotty problem of what function they are meant to fulfil. But the AAAS, again like the BA, may itself be destined for yet more changes, for later this year a meeting will be held to discuss the future of the association and its annual meetings. That, indeed, was one theme which was often discussed last week, both in the programmed sessions and outside them.

As for the meeting itself, the event which led to the arrests was an extremely silly affair. The AAAS board of directors decided in advance of the meeting that it would take a stronger line this year against any radicals who disrupted sessions, and as a first step it forbade any organization not affiliated to the AAAS to set up literature stalls or distribute leaflets. SESPA decided, however, to ignore the ban and, as it has in the past, set up a stall in the registration area from which to peddle its wares. After a day of bickering, Dr Richard A. Scribner, the meeting director, called in the police to remove the table. Scuffling broke out and seven scientists and a reporter were arrested. SESPA screamed about freedom of speech, but Scribner replied that everybody has a chance to be heard in the meetings, and that rules are rules. In the meantime, SESPA was offered, and later grudgingly accepted, a table in a less conspicuous place. The result: AAAS officials provided SESPA with great publicity and eight people have been charged with disorderly conduct.

Another potentially explosive situation was headed off later in the week when Dr Daniel P. Moynihan decided for the second year in succession to miss a meeting rather than face an unruly audience. Moynihan was due to chair a meeting on public policy and social science, but cried off because he said he had to go to a briefing at the State Department on his new appointment as Ambassador to India. He was, however, bitterly attacked in a leaflet distributed throughout the conference in the morning—it was alleged that his work for the White House has led to cutbacks in services to minorities—and the meeting of which he should have been chairman was overflowing. Dr Harold Orlans, a member of the Brookings Institution and one of the panellists at the meeting, later rebuked Moynihan for finding an hour to have lunch with the panel, but not even half an hour to discuss his views with the rest of the meeting. The session eventually proceeded with only minor disruption.

Apart from those few distractions, participants in the meeting were fed a diet of lectures and symposia which, although increasingly concerned with issues of science and society, are still heavily weighted towards the presentation of scientific papers supposedly dealing with topics of general public interest, but often attended only by specialists. This year's meeting was split in the ratio of about 60 per cent scientific symposia, about 30 per cent symposia dealing with issues of science and society, and the rest of the meetings were concerned with Washington-area topics, such as community education in Anacostia.

But the meeting also marked a turning point in the association's history, for at a council meeting held on the last day, a set of by-laws was adopted which will allow the new constitution to come into effect on January 15. The AAAS is at last going to become more democratic. Approved at the annual meeting in Philadelphia a year ago, the new constitution provides for the chief officers of the AAAS to be elected by mail ballot of all the members and for the council to be reduced in size and also directly elected by the membership. Previously, the president and board of directors were elected by the council—an undemocratic procedure which has long drawn sharp criticism.

Largely the work of a committee which met under the chairmanship of Dr Leonard Rieser, a physicist from Dartmouth College, who will become president of the AAAS on January 15, the new constitution drastically reduces the size of the council, from more than

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AAAS Opposes the War

IN the dying hours of the conference last week, the AAAS Council took the unprecedented step of harshly criticizing US policy in South-East Asia. The council called for immediate withdrawal of US troops from Vietnam, Laos and Cambodia, and urged that a full scale study be conducted of the long-term effects of the bombing, the use of CS and of herbicides and other methods of defoliation, both on the people and the ecology of Vietnam. The AAAS council specifically threw its support behind a bill introduced into Congress last session by Senator Gaylord Nelson and Representative Gilbert Gude, which calls on President Nixon to ask the National Academy of Sciences to carry out such a study.

Although the Vietnam war has been a chief focus of the protests of radical scientists at AAAS meetings, anti-war groups have in the past been unable to steer such strongly worded resolutions through the council. Three years ago, however, the council did set up a commission to study the effects of herbicides in Vietnam, the results of which played a part in persuading the Department of Defense to phase out the use of chemical defoliants in the war. What the association is now requesting is that a commission be set up much like the US Atomic Bomb Casualty Commission, which made a long-term study of the effects of the atomic bombs dropped on Hiroshima and Nagasaki in the Second World War. The chief sponsor of the resolution was Dr E. M. Pfeiffer, of the University of Montana, who was also chiefly responsible for persuading the council to undertake the previous study of defoliants. The war will be on the agenda while it lasts.

500 members to about 100, and makes it more responsive to the wishes of AAAS members. In the past, the council has drawn its members from the officers of the AAAS, representatives of the association's twenty scientific sections and delegates from the 300 or so societies which are affiliated to the AAAS, a fact which effectively puts the control of the association in the hands of the affiliated societies and not necessarily in the hands of paid-up AAAS members. The by-laws adopted last week, however, put the control back where it belongs—at least in theory. The net effect of the new constitution, Dr Rieser said last week, is to "provide a vehicle whereby the association is more responsive to its members, who would be more than just subscribers to *Science*". But will the newly democratized AAAS change its role, branch out into pastures new, or even change the format of its annual meetings? Like other scientific organizations, the AAAS is now having to examine its *raison d'être,* and to find ways to be responsive to the changing climate in which science is conducted. Over a hundred years ago, when the association was first formed, its role was simple—it was a primary means of communication among scientists and between scientists and the general public, but now that scientific journals, and to some extent meetings of learned societies, provide the primary channels for communicating research results, the AAAS and in particular its annual meeting are increasingly having to take on other roles.

That much was realized more than 20 years ago, for the AAAS board of directors held a meeting in 1951 to discuss the role that the association should try to play in the decade then ahead. The recommendations were that the AAAS should devote less energy to the detailed aspects of science and pay more attention to problems concerning science, technology and their relations with society, and since then there has been a gradual increase in the general symposia served up at the annual meetings. The officers of the association have now decided, however, that it is time to take another look at the aims of the AAAS and have called a second meeting for October this year. That meeting, to be called the Second Arden House Conference, will present a report to the council at the 1974 annual meeting.

Dr Rieser expects this conference to address three chief issues. How can the AAAS incorporate the technological community into its activities—at present the association is chiefly concerned with and draws its members from the scientific community? How can the association better carry out its objective of increasing public understanding of science? And how can it play a more effective role in making sure that science is used to increase public welfare? In particular, Dr Rieser said that the conference will be concerned with the role that the AAAS should play in the legislative process.

Those questions were given something of an airing during the annual meeting last week at a symposium entitled "Professional Societies in the Process of Change". But a question often asked outside that symposium was what is the function and the product of the annual meeting itself? It is estimated that about 8,000 scientists, and others passed through the meeting, some drawn by the specialized symposia, others attracted to the sessions on more general topics, but the most common opinion was that little that was new emerged.

The chief value of the meeting may be, as Dr Rieser maintains, to provide a forum in which "A lot of people of consequence engage in debate and interaction with each other". He also pointed out that the participants are drawn from all scientific disciplines as well as from outside science itself, and that is a feature which no other major conference in the United States can claim. Moreover, Dr Rieser defended the mix between specialized scientific symposia and sessions devoted to science and society on the ground that the specialized meetings are valuable in bringing scientists up to date with advances in fields outside their own.

Whatever the Arden House Conference may recommend about the structure of the annual AAAS meeting, however, it is already due for change. It is being moved away from its traditional time between Christmas and the new year. The next meeting will be in June in Mexico City, then it will move to a permanent date in late winter. The 1974 conference, for example, has been scheduled for February in San Francisco.

Elected President

ALTHOUGH the new AAAS constitution is not yet in force, the council decided to bring in one provision a year early. The president-elect was chosen by mail ballot of all the members and simply ratified at the meeting last week. The first AAAS president to be chosen directly by the membership of the association will be Dr Roger Revelle, director of the Center for Population Studies at Harvard University, who will take up office in January 1974. About 35,000 of the 130,000 AAAS members exercised their new electoral power.

INDUSTRIAL RESEARCH

New Brooms for Good

DR LEWIS M. BRANSCOMB, now chief scientist for IBM, last week launched a sober, but nevertheless effective, attack on the federal government's policies for stimulating industrial research and development. The effectiveness of his attack stems not so much from what he said but from the fact that he was at least partly responsible for putting the policies together. He was director of the National Bureau of Standards until he left to join IBM last summer. Branscomb's argument is that the Administration has failed to build on the policy basis set out in the President's Message on Science and Technology (delivered in March last year) by refusing to spend money appropriated by Congress for programs designed to help remove barriers to industrial innovation.

The chief target of Dr Branscomb's attack, delivered during a session of the AAAS meeting, was the Experimental Technology Incentives Program (ETIP), which is designed to pinpoint the barriers to innovation and experiment with methods for removing them. Jointly administered by the National Science Foundation and the National Bureau of Standards, ETIP is one of the chief products of the planning exercise headed by Mr William Magruder and other members of the White House staff in 1971 which tried to find methods to stimulate civilian research and development. He said that the ETIP programs are neither "well defined nor understood and the effect of their establishment has been to slow down excellent programs already doing the job".

Dr Branscomb announced that the Office of Management and Budget has impounded funds for the present year for the National Bureau of Standards, so that the bureau is allowed to initiate only one new program, ETIP, and that has been allowed only 14 per cent of the funds requested from Congress. The effect has been to squeeze many of the bureau's established programs, designed to solve existing industrial problems. "It is very disappointing to see a pattern of successful work in support of economic development and public protection, welcomed by the industrial R and D community, turned off and replaced by a speculative program whose basis for usefulness is still to be established", he said. A spokesman for the Office of Management and Budget refused to confirm or deny Branscomb's allegations, but said that the amounts of money to be impounded in the present fiscal year have not yet been decided for all agencies. The Administration's budget for 1974 is released later this month.

NEWS AND VIEWS

Discoveries of New Radio Stars

THE first surveys of the radio sky revealed many radio objects but none was found in the position of a star visible to the naked eye. These first radio sources were referred to as dark stars. The earliest identifications were made with optical nebulae—supernova remnants, ionized hydrogen clouds around young stars and eruptive or peculiar galaxies. Indeed a simple calculation readily shows that the blackbody radiation from the optical disk of a star, whether it is a very bright O or B star or a red giant of large diameter, would be far below the limits of detection. Stars were then dismissed as being of no interest to radio astronomy.

Many years later two theoretical papers showed that under favourable conditions radio emission might be detectable from certain types of star. Schatzman in 1958 pointed out that because the radio emission from the Sun at the time of a flare can increase by factors of 10^6 or more above the quiet Sun value it should be possible to detect the radio emission from flare stars which erupt into even more violent flare activity than the Sun. Such radio burst emission was found by Lovell at Jodrell Bank and Slee and colleagues at Sydney.

The other prediction was made by Weyman and Chapman in 1965 who pointed out that certain red giant stars had absorption lines with blue shifted structure which indicated a flow of gas from the star. Weyman and Chapman argued that this gas would be hot and would form an extensive envelope around the red giant making it detectable at short radio wavelengths; it would be more difficult to see at longer wavelengths because this envelope would be optically thick. On page 37 of this issue of *Nature* Altenhoff and Wendker report the first detection of a red giant (Betelgeuse=α-Orionis) using the 100 m radio telescope which has recently been built at the Max Planck Institute for Radio Astronomy at Bonn. Previous attempts to detect Betelgeuse have been unsuccessful or uncertain because of the poorer sensitivity of the smaller telescopes or the low frequencies used. The Bonn results show that Betelgeuse gives a signal of 8 ± 1 milli flux units (10^{-29} W m^{-2} Hz^{-1}) at a frequency of 10.7 GHz. This flux is consistent with emission from the corona of the star. It is also interesting that Betelgeuse is an infrared source, which implies that the outflowing gas condenses to form a circumstellar cloud of dust grains.

Another group of stars has recently been discovered by Wade and Hjellming using high sensitivity aperture synthesis techniques at the National Radio Astronomy Observatory in West Virginia. These are all eclipsing binaries in which the emitting star is of spectral type B. In all cases there is clear evidence for an outward streaming of gas from the surface of the star. The stars in this class are α-Sco (Antares—the blue component of the double star system), β-Per (Algol), β-Lyr and the star associated with the X-ray source, Cyg X-1. These four sources have a quiet state flux at 8 GHz of about 10 milli flux units, but show in addition marked irregular increases in brightness which are probably associated with the ejection of material from the star and consequent changes in the radio opacity.

The radio emission from another star, No. 349 in the Mt Wilson Catalogue, is also described in this issue. MWC 349 is rather difficult to classify because it lies behind about 10 mag of absorption in the constellation Cygnus where it most likely belongs to the Cygnus OB2 association. It is an emission-line B star which shows gas emission from its surface and has many similarities to the eclipsing binary B stars described earlier. Infrared observations suggest that it is surrounded by a dust cloud. The first radio detection of MWC 349 was made by Braes, Habing and Schoenmaker (*Nature*, **240**, 230; 1972); the new observations reported on pages 37 and 38 by Altenhoff and Wendker at 10.7 GHz and by Baldwin, Harris and Ryle at 5.0 GHz (using the 5 km aperture synthesis telescope at Cambridge) give a much clearer picture of its nature. Its radio flux continues to rise towards higher frequencies indicating that it is radiating by free-free emission from an optically thick gas cloud with an electron temperature of $9{,}000 \pm 2{,}000$ K. The Cambridge radio astronomers were able to measure the angular diameter (2.4 arc s), and thereby estimated the mass of the emitting cloud to be 9×10^{-3} solar masses. Baldwin *et al.* point to the similarity of the radio continuum properties of MWC 349 with those of the continuum source associated with the OH masering object W3 which is thought to be the HII region around a recently formed star still embedded within the parent gas cloud.

There is clearly a reawakening of interest in stars among radio astronomers who are being encouraged by the high sensitivity of the new breed of filled and unfilled aperture radio telescopes which make feasible the detection of weak emission from the circumstellar gas. The objects detected so far are a fascinating collection—red giants, blue emission line stars with P Cygni type line profiles, X-ray sources, and compact clouds of gas, molecules and dust around recently formed stars. Radio observations are likely to provide important information about the evolution of these objects.—R. D. D.

DMN and Cervical Cancer

THE finding of what might have been dimethylnitrosamine (DMN) in pooled human cervical and vaginal discharge matter by J. S. Harington and his colleagues (see page 49 of this issue of *Nature*) raises several matters that merit discussion. First, although the study involved the examination of vaginal fluid from a hundred African women, the fact that the specimens were pooled for the purposes of chemical analysis means that the report constitutes no more than a single unconfirmed observation. In spite of the care taken in the collection of specimens the possibility of contamination of one or more of them cannot be ruled out, and even if it could, one is not to know whether the DMN allegedly found in the pooled material came from several or only one woman. Nor can it be assumed that DMN found in vaginal fluid is the result of synthesis by microbial action in the vagina. For one reason or another various objects and chemical preparations find their way into the vagina so that the possibility of contamination of the vagina by exogenous DMN cannot be excluded.

Harington *et al.* refer to the fact that, under acid conditions, nitrosamines can be formed by the reaction of nitrites with secondary amines. This has been shown to take place, for example, in the acid conditions of the stomach (W. Fiddler *et al., Nature,* **236**, 307 ; 1972 ; and W. Lijinsky *et al., ibid.*, **239**, 165 ; 1972) and during the processing of nitrite-preserved herring into fish meal (F. Ender *et al., Z. Tierphysiol., Tierernähr Fullermittelk.*, **22**, 189 ; 1967). It has also been shown that nitrosamines can be formed from secondary amines and nitrates under neutral conditions in the presence of nitrate-reducing bacteria, including some strains of lactobacilli, group D streptococci, clostridia, bacteriodes and bifidobacteria (J. Sander, *Hoppe-Seyler's Z. Physiol. Chem.*, **349**, 429; 1968). The *p*H and temperature of the infected vagina are theoretically conducive to nitrosamine formation, but there are no very obvious sources of nitrites or secondary amines. It is possible that, as in the case of saliva (personal communication from C. L. Walters, British Food Manufacturers' Industrial Research Association), nitrites are present in low concentrations in vaginal secretions and that traces of dimethylamine are formed from lecithin present in the vaginal epithelium, but in neither case are the amounts likely to be adequate for significant nitrosamine formation. Nitrates present in urine might be reduced to nitrites by the microflora of the vagina, but one would not expect appreciable quantities of urine to find their way into the normal vaginal vault. Unless secondary amines and nitrites are introduced into the vagina for contraceptive or other purposes it is difficult to envisage why either should be present there except in trace amounts.

Harington *et al.* undertook their study as part of an investigation of the causation of cervical cancer in Southern Africans among whom the disease is common. Studies of other ethnic groups have indicated a relationship between risk of cervical cancer and sexual activity, multiplicity of sexual partners, coitus with uncircumcised males and poor standards of hygiene. There is no particular reason to think that different factors are responsible among Southern Africans. The question which the possible finding of DMN in vaginal fluid raises, therefore, is whether DMN formation is a part of the mechanism by which poor sexual hygiene increases cancer risk. There can be no doubt that exposure to DMN may increase the risk of cancer development in many animal species, but there is no evidence from animal studies that its introduction in the vagina predisposes to cancer of the cervix. This is perhaps an experiment that should now be undertaken. *A priori,* however, one would not necessarily expect intravaginally administered DMN to lead to cancer development in the cervix. It is generally agreed that its carcinogenic activity depends on prior conversion to the corresponding diazoalkane and it is not certain whether the enzymes needed for this conversion are present in the cervix.

Harington *et al.* did not measure the concentration of the alleged DMN that they found, but presumably it was low. If so, one is bound to wonder whether its presence in trace amounts would have any significance at all. A feature of life today is that the sensitivity of methods of chemical analysis in many areas of toxicology is of a different order than that of the methods available for judging biological effects such as carcinogenic activity. The finding of a potent carcinogen in trace amounts in the vagina of a woman with cervical cancer is as uninterpretable as the finding of C-type particles in a cancer of the cervix. In neither case can a cause and effect relationship be assumed or proved.

For the many reasons given here, no conclusions can or should be drawn at this stage from the reports of Harington and his colleagues. Nevertheless, the authors were right to report their findings because they might be important and others will certainly wish to set about seeing whether they are. The first hurdle is to confirm that DMN may be present in vaginal fluid under certain circumstances; the second is to show that it may be present there in biologically significant amounts; the third is to show that DMN administered intravaginally is capable of causing cancer of the cervix in animals. A fourth and most important hurdle is to find a link between the presence of DMN in the vagina and the development of cancer of the cervix: for example, a relationship has to be demonstrated between the presence of DMN and the presence of cancer, or rather an increased risk of developing cancer, of the cervix. If all these hurdles were to be surmounted, a causal relationship would seem likely, though still not proved. On the basis of the limited information available, some of the hurdles look forbiddingly high.—From a Correspondent.

Eukaryotic DNA Replication

PROGRESS in the investigation of DNA replication in eukaryotes has been confusing and messy. The involvement of a membrane site in DNA synthesis in bacterial cells, first suggested by Jacob, Brenner and Cozin in 1963, prompted a search for a similar mechanism in eukaryotic DNA replication. Two types of investigation have been attempted, producing conflicting results.

First, in cell fractionation experiments with mammalian cells, Friedman and Mueller, Mizuno, Stoops and Sinha, Hanaoka and Yamada and Pearson and Hanawalt presented evidence that newly replicated DNA (detected by pulse-labelling with ^{3}H-thymidine) is associated with membrane material. Its buoyant density in CsCl gradients is lower than bulk DNA and it is located in the phenol-water interphase during phenol extraction. This type of experiment, therefore, suggested that DNA replication sites are located at the nuclear membrane.

In contrast, more electron microscope autoradiographic experiments suggested that DNA replication sites were distributed throughout the nucleus. Comings and Kakefuda, investigating unsynchronized human amnion cells which had been pulse-labelled for 5 min, found label over the whole of the nucleus. When cells which were synchronized in early S-phase were pulse labelled for 5–10 min, however, they found that label was concentrated at the periphery of the nucleus at the beginning of S-phase and only later was label distributed throughout the nucleus. Comings and Kakefuda concluded that initiation of DNA replication took place on the nuclear membrane, whereas replication could occur all over the nucleus. Other authors, however (Williams and Ockey, Erlandson and de Harven and Blondel), found that DNA synthesis in early S-phase occurred all over the nucleus, but that label became concentrated around the nuclear membrane in late S-phase. No shift of label occurred during chase periods with unlabelled thymidine and later peripheral labelling represented replication of heterochromatin close to the nuclear membrane.

All this is very confusing and the basic questions remain unanswered. Does DNA replication occur solely at the nuclear membrane or over the entire nucleus? Does DNA remain fixed in the nucleus while the replication site moves along it, or does the replication site remain fixed while the DNA is displaced relative to it, or do both replication site and DNA move?

On page 32 of this issue of *Nature*, Huberman, Tsai and Deich at last throw some light on this picture of confusion, especially with regard to the autoradiography experiments. The two principal sources of error in previous work have been over-long pulses of labelled thymidine and variation in methods of cell synchronization. Because DNA replicates at a rate of 0.5–1.2 µm/min, a pulse of 2 min and more could result in erroneous location of originally peripheral grains in a central position in the nucleus. All of the previous autoradiographic studies involved pulse times of 5 min or greater.

The amethopterin method of synchronization used by Comings and Kakefuda is now known to cause cellular damage in the form of abnormal nuclear transformation. Thus Tokuyasu, identifying a cell's position in S-phase according to its centriolar development, found that the cells with heavy peripheral labelling identified by Comings as early S-phase were, in fact, late S-phase.

Huberman *et al.* carefully avoided these pitfalls. They used short pulse times of 0.5 min and the much gentler synchronization method of metaphase selection, and found general labelling throughout the nucleus in early S-phase with peripheral labelling becoming predominant in late S-phase. Because it is known that heterochromatin is late replicating, and because Huberman's pictures show a preponderance of condensed chromatin at the nuclear envelope, these results suggest that euchromatin is replicated early in S-phase and is distributed throughout the nucleus, whereas heterochromatin replicates late in S-phase and is located close to the inner nuclear membrane.

Moreover, in unsynchronized cells, Huberman *et al.* found no difference in the location of grains after a 0.5 min pulse, a 10 min pulse and a 0.5 min pulse followed by a 6 h chase and, in synchronized cells, label from a 0.5 min pulse remained unchanged in position after a 6 h chase. They conclude, therefore, that DNA has a stable location in the nucleus.

Finally, Huberman *et al.* suggest that, in the cell fractionation experiments, it is possible that newly replicated DNA may possess special features such as extensive single strandedness which may cause it to bind more protein or membrane material than bulk DNA. Indeed, careful experiments recently reported by Fakan *et al.* confirm that the behaviour of newly replicated DNA in CsCl gradient and phenol extracts is a result of its single strandedness rather than its association with membrane material. They present evidence that newly replicated DNA is not preferentially located with nuclear membranes but is found in a fraction of chromosomal deoxyribonucleoprotein very slightly lighter than bulk deoxyribonucleoprotein and probably consisting of DNA and the additional proteins involved in DNA replication.—From a Correspondent.

TUMOUR VIROLOGY

Mutant Viruses

from our Cell Biology Correspondent

THE first report of the isolation of temperature sensitive mutants of polyoma virus appeared in 1965 and, for reasons that are far from clear, attempts to isolate similar mutants of Simian Virus 40 failed for several years. In the past two years, however, three or four groups have succeeded in isolating temperature sensitive mutants of SV40 and have begun the job of characterizing them. Tegtmeyer, for example (*J. Virol.*, **10**, 591; 1972), has characterized three of his mutants, *ts*A7, *ts*A28 and *ts*A30, which are all in one complementation group and are apparently SV40 equivalents of Fried's *tsa* mutant of polyoma virus, one of the most instructive mutants of this virus. The gene that is defined by Tegtmeyer's three mutants specifies a function that is required for the initiation but not the maintenance of transformation and also for the initiation of rounds of viral DNA replication during the lytic cycle of this virus.

When non-permissive mouse 3T3 cells at 39° C are infected with any one of the three SV40 mutants, the number of cells that are transformed is some 25-fold to 158-fold less than the number transformed after infections at 33° C; the function of the mutated gene is

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Direct Sequencing of Phage DNA

IN next week's *Nature New Biology* (January 10) there is a set of three reports from the MRC Laboratory of Molecular Biology in Cambridge which describe how the base sequences of two fragments of the single-stranded DNA of bacteriophage φX174 have been analysed directly and how one of these sequences has been identified as the 5′-amino-terminal end of the spike protein cistron of the phage genome. Ziff, Sedat and Galibert, working in Sanger's laboratory, used endonuclease IV induced by phage T4 to digest partially φX174 DNA and from the digestion products they isolated a fragment forty-eight nucleotides long. After this fragment was depurinated and digested with snake venom phosphodiesterase, spleen phosphodiesterase and endonuclease IV, the sequences of the oligonucleotides which comprise this fragment were determined by fingerprint analyses. These methods should prove to be of general application for sequencing DNAs.

Robertson, Barrell, Weith and Donelson have also sequenced a fragment of φX174 DNA using some of the methods developed by Ziff *et al.* They isolated a fragment of this viral DNA by first binding ribosomes to the DNA and then digesting away all but the sequence protected by the ribosomes. This technique has, of course, been used to isolate ribosome binding sites of the RNAs of phages R17 and Qβ preparatory to sequencing.

The sequence of the φX174 DNA protected by ribosome binding proved, as expected, to contain a triplet ATG, equivalent to an AUG codon; moreover, if the sequence is arranged to maximize base pairing the ATG triplet occurs at the loop of a hairpin structure. As Robertson *et al.* point out, this and other features of the sequence are shared by the sequences of the initiation sites of the R17 and Qβ phage coat protein cistrons.

All these data indicate that the fragment of φX174 DNA that has been analysed is the beginning of a cistron. In the third article of the set, Air and Bridgen report the amino-terminal amino-acid sequence of the φX174 spike protein specified by cistron G. This amino-acid sequence is precisely that predicted from the nucleotide sequence reported by Robertson *et al.*, who have clearly isolated and analysed the first part of the φX174 G cistron.

therefore required to initiate transformation. When permissive African green monkey cells of the AH line are infected at 33° C, 39° C and 41° C with these mutants the yield of infectious SV40 particles is 10-fold less at 39° C than at 33° C and about 10^4 less at 41° C than at 33° C. Moreover, the amount of infectious DNA that can be extracted from cells at the higher temperatures is commensurately lower. The mutant virus particles are not themselves more thermolabile than wild type virus particles, and this indicates that the mutated gene probably does not specify a structural protein of the virion, and that infections with naked mutant DNA, like infections with mutant particles, are temperature sensitive. It would seem, therefore, that adsorption and uncoating of these mutant particles are not temperature sensitive events.

To investigate further the temperature sensitive function Tegtmeyer infected AH cells at the permissive temperature. After replication of the viral DNA had started he shifted the cells to 41° C and fed them 10-minute pulses of ^{3}H-thymidine. Viral DNA was then extracted from the cells and analysed by gel electrophoresis, using a technique that Tegtmeyer and Macaset (*J. Virol.*, **10**, 599 ; 1972) have devised. Tegtmeyer concludes, from the pattern of incorporation of label into progeny SV40 DNA during such shift-up experiments and during shift-down experiments, that at the non-permissive temperature DNA molecules partially replicated at 33° C can be completed but that new rounds of replication cannot be initiated. In other words, Tegtmeyer's experiments clearly indicate that the *tsA* gene of SV40 specifies a specific initiator of viral DNA replication and presumably the same is true of the *tsa* mutant of polyoma virus. Needless to say, the protein specified by this gene has not yet been isolated, but it will not be surprising if it proves to be either an endonuclease or a protein capable of denaturing double-stranded DNA because either or both of these activities may be required to initiate viral DNA replication and integration of viral DNA into host cell DNA.

In the same issue of the *Journal of Virology* (page 653) Scolnick, Stephenson and Aaronson report the isolation of mutants of murine sarcoma virus which carry a lesion(s) in a gene(s) required for the maintenance of transformation. They obtained mutagenized stocks of Kirsten mouse sarcoma virus by exposing to bromodeoxyuridine rat cells, which were supporting the replication of this virus together with murine leukaemia virus. They then infected NRK rat cells with limiting dilutions of the mutagenized KiMSV (MLV) and isolated clones of transformants using microwell plates. By replica plating these transformants at 32° C and 39–40° C Scolnick *et al.* detected three lines (out of 3,000 tested) of transformants which, as judged by colony morphology, were temperature sensitive for transformation. The transforming sarcoma virus genome was rescued from these non-producer cells by superinfecting them with murine leukaemia virus. Two of the three rescued sarcoma viruses proved to give rise to temperature sensitive transformants.

Hybridization tests proved that KiMSV RNA is synthesized in similar amounts in cells transformed by these viruses and grown either at 32° C or 39° C. Transcription is not, therefore, temperature sensitive. Apart from that, these mutants have not been further characterized, but Scolnick *et al.* say they intend to isolate a suite of such mutants and by complementation tests determine how many MSV genes are involved in maintaining transformation.

SPIN LABELS

Radical Solutions

from our Molecular Biology Correspondent

THE spin-label technique has been applied with discrimination and elegance to several systems by McConnell and others. For placing this instrument into so many hot and eager little hands, however, its inventors will have to answer to their consciences, for a rash of electron spin resonance (ESR) spectra is now spreading like a contagion through the biochemical literature. Spin labels being commercially available, sensitive to the smallest kind of environmental change, and the ESR experiments technically undemanding, it is now possible to generate mountains of data with rather little effort, and the comfortable conviction that even if it is by no means obvious what they mean, they must assuredly mean something.

Through the gathering fog one may, however, discern some new and potentially useful ramifications of the method, as regards, for example, the measurements of critical distances. Two unpaired spins sufficiently close together will interact, and the perturbation of the ESR spectrum can be analysed in terms of the distance between them; second, NMR signals are also apt to be broadened if the nuclei from which they arise are in close proximity to a paramagnetic centre. The second method has been explored by a group in Oxford, and an interesting approach to the potentialities of the first has now been made by Russian workers.

The story is to be found in two articles just out. Kokorin *et al.* (*Biophysics*, **17**, 34; 1972) have examined the effect of intermolecular distance on the ESR spectra of a series of iminoxyl derivatives in solution at low temperature. These conditions, including the use of glassy solvents, such as water-glycerol mixtures, are chosen to allow the observation of dipole–dipole interactions, in the absence of the otherwise important exchange contributions. As the concentration of the radical increases, the average intermolecular distance becomes small enough for dipole–dipole broadening and splitting to

Aminoacyl-tRNA Synthetase in RNA Tumour Viruses

RNA tumour virus particles have been shown to contain a variety of enzymatic activities and several sorts of nucleic acids, including some forms of host tRNAs, that are accumulated in a non-random way presumably as the virus particles bud from the surfaces of productively infected cells. These viruses also contain some ribosomes of the host cell.

It is not yet understood why the RNA tumour viruses should sequester parts of the protein synthesizing machinery of the host cell, nor is it known whether they function to make protein after they are incorporated into the virions, but the list of components discovered in these viruses continues to lengthen. Trávníček and Říman, for example, as they report next Wednesday in *Nature New Biology* (January 10), have now detected aminoacyl-tRNA synthetase in avian myeloblastosis virions.

In avian myeloblastosis virus particles lysine tRNA is more abundant than any other species of tRNA, although that is not the case in the cells in which this virus replicates. Trávníček and Říman therefore assayed virions disrupted by the non-ionic detergent 'Nonidet' for an aminoacyl-tRNA synthetase capable of charging lysyl-tRNA with lysine, and sure enough they found such activity. Furthermore, comparisons of the aminoacyl-tRNA synthetase activities for leucine, lysine and valine in AMV particles and in host cells indicate that both lysine tRNA and lysyl-tRNA synthetase are preferentially accumulated in the virus particles.

As Trávníček and Říman comment, the selective rather than random sequestration of particular components of the host cell's protein synthesizing machinery by these viruses suggests that the process may not be fortuitous. And if it is not fortuitous these molecules must presumably function at some stage in the life history of the virus particles; precisely when has yet to be determined.

manifest itself. A simple quantitative measure of the resulting perturbation of the spectrum is the ratio of the amplitude of the central line to that of one of the hyperfine components. The broadening, and also, where it can be observed, the dipole–dipole splitting, depend on the inverse-cube of the separation, which can therefore be determined.

For a series of iminoxyl biradicals, in which the two paramagnetic centres are separated by structures of varying length, the separations so derived agree to about 1 Å with those based on the concentration calibration for monoradicals. For oxyhaemoglobin bearing a spin label on a β-chain thiol group, the line-width parameter is the same as for the free label, whereas the same radical attached to methaemoglobin displays broadening, in consequence apparently of interaction with the high-spin ferric haem iron atom. With two iodoacetate-based spin labels, one on each β-chain of oxyhaemoglobin, there is again no broadening, in accordance with the large separation of the two thiols in the molecule. If, on the other hand, a second label is introduced by way of a cyanuric fluoride derivative, which is thought to react with a histidine, interaction between this and the paramagnetic label on the thiol is observed, to an extent that indicates a separation of 25 Å. The size of the label makes this a somewhat vague parameter, and it is in any case at the upper distance limit of sensitivity. When the protein is denatured, however, the separation appears to decrease by 3 Å.

In an accompanying article (Kulikov *et al.*, *ibid.*, 40), the intramolecular interactions of a series of biradicals, mostly on rigid skeletons, are observed by the broadening of ESR signals from glassy low-temperature solutions, using the second moment of the spectrum as a criterion. The interaction falls off in the expected manner with separation, being very large at 12 Å, and barely measurable at 18 Å. The agreement between the separations, as calculated from the broadening and measured on molecular models, is remarkably good. Compounds containing more than two radicals, and even a copolymer of styrene, acrylic acid and an iminoxyl derivative, have also been examined in the same way. Interactions between spin labels on various groups of proteins are described; for example, the distance between the two reactive thiols needed for ATPase activity of myosin has been estimated at 14–18 Å.

A similar approach to the measurement of distances between labelled molecules in a phospholipid bilayer has been explored by Marsh and Smith (*Biochem. Biophys. Res. Commun.*, **49**, 916; 1972). Spin-labelled cholestane introduced into bilayers at sufficient concentration shows large dipole–dipole splitting when the magnetic field is perpendicular to the planes of the stacked bilayers. The separation of the labelled molecules in the plane is calculated from the splitting, and is found (not surprisingly) to vary with the composition of the phospholipid. In saturated phospholipid bilayers the spin-labelled species are close together, whereas the introduction of cholesterol drives them apart.

This general approach to the measurement of distances between groups capable of accepting a spin label may turn out to have considerable advantages over measurement of electronic excitation transfer. Whether it too will remain a technique of primarily decorative rather than utilitarian value in regard to real biological problems will remain to be seen. One has learned to read the signs in the lofty phrases, usually to be found at the ends of papers, regarding the promise and scope of whatever new method has just been trundled onto the launching pad.

DESERT ANIMALS

Avoiding a Salty Diet

from our Animal Behaviour Correspondent

THE harsh environment of the desert poses many problems, such as those of combating heat and obtaining enough food and water, to animals like the kangaroo rats (Heteromydae) which live in the deserts of western North America. The possibility of obtaining food and water from such plants as can survive there is confounded by the fact that one of the adaptations shown by desert plants such as the saltbush (*Atriplex*) is to have a layer of salt-filled tissue at the surface of their leaves. This seems to help the salt-water balance of the plants but would make them dangerous eating for most animals because of the high concentration of salt. In one species of kangaroo rat, *Dipodomys microps*, this particular difficulty has been partially solved by the evolution of specialized teeth and behaviour which help to provide it with a year round supply of food.

G. J. Kenagy reports (*Science*, **178**, 1094; 1972) that this species has broad, chisel-shaped lower incisors, unlike other species of kangaroo rat living in the same area, which have relatively narrow and rounded lower incisors. Chisel-shaped lower teeth enable it to strip off the salty outer layers of the leaves and obtain the inner portions of the leaves which are relatively salt-free.

D. microps holds a saltbush leaf in its forefeet and draws it over its lower teeth about ten times, so shaving off the outer layers of one side. It then turns the leaf over and does the same thing to the other side. Kenagy found that the discarded shavings are very high in electrolytes and are not eaten by the rats, whereas the sodium concentration of the inner tissue, which the rats eat, was only 3 per cent of that of the shavings. Furthermore, in a feeding experiment, Kenagy found that *D. microps* could survive for at least 16 days on a diet of nothing but saltbush leaves. A closely related species, *D. merriami*, would not eat these leaves and died within 2 days.

Saltbush leaves are available all year round, so that *D. microps* is provided with a predictable and continuous food supply. This minimizes competition with closely related species which subsist on seeds, but for whom the saltbush is like the water, water everywhere of the Ancient Mariner.

Homology of Fungal and Mammalian Protein

THE sequence of the enzyme glutamate dehydrogenase from bovine liver is known from the work of Smith and coworkers. These workers also showed that there is little divergence between this and the corresponding protein from chicken, only twenty-six substitutions being found in the 500 residues. Now Wootton, Chambers, Taylor and Fincham report in next Wednesday's *Nature New Biology* (January 10) their comparison of the NADP-dependent glutamate dehydrogenase of *Neurospora crassa* with the mammalian species.

Wootton *et al.* sequenced tryptic peptides and tried to index each of them on the sequence of the bovine liver enzyme. In general a unique best-match was found, with a vanishingly low statistical probability that it would have occurred by chance. There is a lysine in a position corresponding to the reactive lys-126 of the bovine sequence, and a general sequence homology around it extends the observation of a similar centre in the sequence of bovine glyceraldehyde 3-phosphate dehydrogenase.

Some *Neurospora* mutants were also examined, and it seems that a cluster of basic residues, his-lys-his, is somehow involved in stabilizing the enzymatically active conformation of the protein, for replacements in this position lead to anomalous activation behaviour. The existence of distinct homologies in many parts of the *Neurospora* and bovine glutamate dehydrogenase sequences is taken to signify a common evolutionary origin, rather than evolutionary convergence.

ULTRASOUND

Clinical Applications

from a Correspondent

THE multidisciplinary nature of ultrasonic techniques in medicine was well illustrated at a conference held at the Welsh National School of Medicine, Cardiff, on December 15. The value of diagnostic ultrasound in obstetrics has now been established, and the precision possible with current methods in detecting and recording the foetal heart from the seventh week of pregnancy was described by Dr H. P. Robinson (University of Glasgow). Considerable accuracy has been claimed for the measurement of the biparietal diameter of the foetal skull *in utero,* which provides important information on foetal gestation and growth. It was, however, pointed out by Dr D. Watmough (University of Aberdeen) that there are certain pitfalls for the unwary. He demonstrated that it is possible to obtain a variety of midlines corresponding to differing diameters of the foetal head. He emphasized the dangers of relying on a simple reading and concluded that both maturity and growth should be assessed by serial measurements over an extended period.

The significance of antenatal bleeding in various stages of pregnancy can be difficult to assess clinically. Dr Margaret Jones (Welsh National School of Medicine, Cardiff) showed that ultrasonic techniques have a valuable part to play in the management of patients who are bleeding in the first trimester to confirm the presence of a continuing normal pregnancy, or to detect a missed abortion or a hydatidiform mole. In the second and third trimesters accurate localization of the placental site is possible. It was pointed out that it is not sufficient to localize the inferior pole of the placenta accurately in early pregnancy as the placenta rises in late pregnancy.

Dr D. A. Carpenter (Commonwealth Acoustic Laboratories, Sydney) provided an exciting glimpse into the future of the art by describing a series of developments aimed at improving the information content without the use of computers. The resolution has been improved by the technique of film echography using a non-storage display tube. A substantial improvement was obtained in the grey scale and the amount of low level echoes displayed on the echogram. Further improvement in the resolution was achieved by the use of medium focused transducers. Further developments are envisaged, which will involve increasing scanning speed and electronic steering and focusing of the ultrasonic beam.

There is, of course, considerable interest in the use of computers in ultrasonic examinations, and a report by Drs R. A. Mountford and M. Halliwell (University of Bristol) of ultrasonic liver and kidney scanning with the aid of off-line computation was of particular value. They have constructed an automated system of data acquisition with direct computer-compatible output and have been able to confirm that the mean echo amplitude was considerably increased in liver cirrhosis. By using off-line computational techniques in an array scanning system, information from the focus can be digitized and stored. Subsequent analysis yields a contour type C-scan display.

Dr R. B. Pridie (London) described how the ultrasound cardiogram could measure the rate of closure of the mitral valve during diastole. The rate of closure is slow in mitral stenosis and in hypertrophic cardiomyopathy. The diastole closure rate is increased in mitral incompetence and in congestive cardiomyopathy. He concluded that if the pulmonary vein pressure is known, a measure of the left ventricular compliance could be obtained using the diastolic closure rate of the mitral valve as the only other parameter.

The manner in which a tissue returns ultrasonic echoes may reflect features of its structure. Drs R. C. Chivers and C. R. Hill (Institute of Cancer Research, Sutton) described an experimental study involving a new approach in which the spectral distribution of the returning echoes from various tissues was analysed.

Japanese workers have for some time described the use of ultrasonic techniques in the detection of gall stones. These results have been confirmed by Dr I. H. Gravelle (Welsh National School of Medicine, Cardiff). He described how gall stones could be diagnosed, but pointed out that small stones could not at present be detected unless grouped together. The method can be used to treat

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Origins of Malignant Lymphoid Cells

THE discovery of distinctive cell surface antigens on thymus-dependent lymphocytes (T lymphocytes) and thymus-independent lymphocytes (B lymphocytes) has provided methods for investigating the organization and function of normal lymphoid tissues. Distinctive cell surface antigens on T and B lymphocytes are detected with specific allo or hetero-antisera and have been identified in several species including chicken, mouse, rat, guinea-pig, and man. Recently such antisera have been used to identify the possible origins of malignant lymphoid cells.

One such study of lymphomas induced in chickens by Marek's disease herpes virus is reported by Hudson and Payne in *Nature New Biology* next week (January 10) and indicates that most lymphoid cells within the lymphomas carry T lymphocyte antigens. This, and their previous observation that chickens having only T lymphocytes (achieved by neonatal bursectomy and X-irradiation) failed to develop lymphomas after infection with Marek's disease virus, suggests that the target cell for the virus is a T lymphocyte. Further support for this hypothesis must await an answer to the question whether or not the T cells in the lymphomas are transformed and carry virus-induced tumour-specific antigens. The RNA leukosis viruses also induce lymphomas in chickens, but the target cell in these lymphomas is probably a B lymphocyte, for early bursectomy prevents lymphoma induction (Cooper *et al., J. Nat. Cancer Inst.,* **41**, 373 ; 1968).

Murine leukaemias have been examined for T lymphocyte alloantigens (θ, TL, LyA, LyB, LyC, LyD) and for B lymphocyte hetero-antigens (MBLA) and surface immunoglobulins (Ig). Many of the murine leukaemias induced by the oncogenic RNA viruses have θ, TL, LyA and so on, and are thus likely to be of T origin. But very few murine leukaemias have been identified which lack T markers yet have B markers. The murine myelomas do not have T markers but do have B markers such as the alloantigen PC, the heteroantigens MSPCA and MBLA, and surface Ig (Shevach *et al., J. Immunol.,* **108**, 1146; 1972).

Markers for human T and B lymphocytes are only now becoming available. The best characterized marker is surface Ig, which is detected on B lymphocytes with anti-Ig serum (20 to 30% of normal blood lymphocytes have surface Ig). Most of the blood lymphocytes of patients with chronic lymphatic leukaemia (CLL) have surface Ig of the IgM class and lack T antigens (as detected with hetero-antisera) (Wilson ond Nossal, *Lancet,* ii, 788 ; 1971). It seems likely that CLL is a disease of the B lymphocyte series. Because T lymphocyte markers are not yet readily available or standardized, the origins of lymphoid malignancies lacking surface Ig have not been determined.

The data so far available suggest that lymphoid malignancies may arise at several stages during lymphocyte differentiation. Antigenic characterization of malignant lymphoid cells will provide an additional means of classifying these diseases, and may provide a basis for studies of interactions between carcinogen and target cell.

patients with obstructive jaundice.

Finally, the conference had a timely reminder from Dr Mary Dyson (London) of the possible risks of ultrasonic scanning. She described experiments in which chick embryos were irradiated at the head process stage. Certain dose parameters produced a significant increase in abnormalities, particularly of the central nervous system. At diagnostic levels no harmful results have been reported, but the field is not yet fully explored.

CHEMISTRY

Asymmetry of C-F

from a Correspondent

RECENT work on the fluorine n.m.r. spectra of silver trifluoracetate, $Ag^+CF_3CO_2^-$, by Waugh and his colleagues at MIT (*J. Chem. Phys.*, **57**, 2147 ; 1972) has revealed a remarkable lack of axial symmetry in the chemical shift tensor for the C-F bonds.

A typical C-F bond has avial symmetry, that is all directions perpendicular to the bond are equivalent. More specifically, vector properties such as a bond dipole moment contribution will lie parallel to the bond: likewise a second rank tensor associated with a property such as the optical polarizability is expected to have one of its principal directions parallel to the bond and the other two to be associated with equal principal values and consequently referring to all directions perpendicular to the bond. Such axial symmetry is a necessary property of a model of a bond in isolation, and would be expected to be realistic for real bonds in molecules, at least in the absence of π electron or aromatic effects.

To understand the findings it must be remembered that an n.m.r. chemical shift, the quantity σ in the energy expression, $-\hbar\gamma\mathbf{I}\cdot(1-\sigma)\cdot\mathbf{B}$, relates to the departure of the n.m.r. frequency for the substance being studied from that of the bare nucleus or other reference state. For fluorine, σ may reach several hundred p.p.m. and is well known for many liquids. But for liquids the quantity observed is the mean value of σ, that is one-third of the trace (Spur or diagonal sum) of the tensor quantity. With very few exceptions these mean values are the only quantities that have been available. The fuller information could not be obtained from solid state spectra because it is normally obscured by the dipole–dipole coupling between nuclei; this is a much bigger effect than the chemical shift and leads to line widths of the order of 10 kHz.

Waugh and his colleagues used a special sequence of radiofrequency pulses to excite the resonance and to remove the effect of the dipole–dipole coupling. The line widths were 0.5 kHz or less, thus enabling the details of the chemical shift to be made plain. In a single crystal of $Ag^+CF_3CO_2^-$, at least at 40 K where the $-CF_3$ rotational motion has been frozen, each distinct C-F bond in the unit cell may make a different angle with the magnetic flux density and consequently have a different effective chemical shift for the fluorine resonance. Six lines were resolved and measurements at several crystal orientations with respect to the magnetic field allowed the complete chemical shift tensor to be derived for each of the C-F bonds of the $-CF_3$ group. There are small, yet real, differences between the bonds, but essentially the results indicate, for each C-F bond, that the principal values and principal axis directions of the σ tensor are +73 p.p.m. along the bond, −75 p.p.m. in the CCF plane and +2 p.p.m. in the circumferential direction around the $-CF_3$ group.

Such a tensor is clearly not of the expected axial type, which would require principal values in the ratios +74: −37: −37. This is surprising, for the electrons in the immediate vicinity of the nucleus normally dominate its chemical shift. Theoretical chemists will have to get to work to explain the lack of axial symmetry and the differences between the three bonds, and to find the reason why the principal direction is actually at an angle of 10° to the C-F bond direction rather than strictly parallel to it.

NUCLEAR PHYSICS

Exchange Effects

EVIDENCE for the occurrence of substantial exchange effects in the elastic scattering of oxygen-16 nuclei from oxygen-18 nuclei is given in a recent issue of *Physical Review Letters* (**29**, 1683; 1972) by Gelbke and his colleagues of the Max-Planck-Institut für Kernphysik at Heidelberg.

It has long been known that, when a light nucleus (typically of mass less than 40 a.m.u.) is scattered from a target composed of similar light nuclei, the observed distribution in angle of the bombarding particles cannot be explained solely by an interaction in which the incident particle is affected by a combination of the Coulomb repulsion between the particles and a nuclear interaction simulated by a potential well with a real and imaginary part (an optical model potential). What the extra mechanism is or what quirk of the mechanism makes the observed angular distribution of elastically scattered heavy particle deviate from that predicted by the optical model has been the subject of considerable speculation. The work of Gelbke *et al.*, however, eliminates some of the suggested possibilities and comes out in favour of an exchange contribution.

The telltale feature of anomalies of this kind in elastic scattering is their variation with the energy of the incident particle. The Heidelberg team studied the reaction of ^{16}O on ^{18}O at 24 MeV.

Oncornaviruses and Breast Cancer

Two of the chief obstacles in the way of further investigations of the virus-like particles which have been detected in samples of human milks and may be human counterparts of mouse mammary tumour viruses are the lack of cultivated cells which can be productively infected or transformed by these milk particles, and the lack of cultures of human breast cells that produce the particles. At present these cells can be obtained only from human milk and there is no assay for their biological activity. The experiments reported in next Wednesday's *Nature New Biology* (January 10) by Keydar *et al.*, however, may show the way to a method of obtaining reproducible cultures of human cells that support the replication of the human "milk virus".

Keydar and his colleagues co-cultivated primary human embryo cells and human breast cancer cells, and exposed other cultures of human embryonic cells to milk, from breast cancer patients, which had reverse transcriptase activity and presumably contained the milk particles. In nine out of a total of fifteen such cultures Keydar *et al.* detected the production of particles which contain 60–70S RNA and reverse transcriptase activity and have a buoyant density of 1.18 g ml. These are, of course, diagnostic properties of RNA tumour viruses. Furthermore, some of these cultures have been producing these particles for nine months whereas control cultures of human embryonic cells not exposed to milk or co-cultivated with cancerous breast tissue have not produced any detectable particles with the characteristics of RNA tumour viruses.

As Keydar *et al.* point out, the particles which are being produced in their cultures may have arisen from the cancer cells and may be involved in the aetiology of breast cancer. On the other hand, they may be contaminants or they may have arisen in the embryonic cells. These second alternatives, however, are less likely and attempts are under way to characterize the particles produced in the cultures and establish their relationship, if any, with virus-like particles in human milks.

28 MeV and 32 MeV—energies close to and slightly above the Coulomb barrier for the interaction of these oxygen nuclei. Gelbke and his colleagues found that at these energies the angular distribution of the scattered particles has two distinct minima in intensity between 90° and 150°; these occurred at approximately the same angle regardless of the energy of the incident particle. This observation immediately rules out explanations of the anomalous behaviour based on the absorption of the incident particle by the nucleus to different extents depending on its angular momentum relative to the scattering nucleus. Thus the anomalous behaviour cannot be explained by an optical model that contains a term which explicitly depends on the angular momentum of the particles, although observations at one energy can be adequately described by such a model.

Gelbke *et al.* think that the incident ^{16}O nucleus picks up the two least bound neutrons in an ^{18}O nucleus and imparts sufficient momentum to the ^{16}O nucleus thus formed for it to emerge from the target. This ^{16}O is, of course, indistinguishable from a normally scattered ^{16}O nucleus.

The experimental angular distributions are fitted by a model which includes contributions from such an exchange mechanism and, as well as reproducing each individual measured distribution at the three energies, the variation with energy is also satisfactorily reproduced. Minor differences in the theoretical fits to the experimental points at the three energies are attributed to the fact that the probability of the incident ^{16}O nucleus picking up the two neutrons from ^{18}O varies with energy.

RADIATION DAMAGE

Precipitate Instability

from our Materials Science Correspondent

It is not at all surprising that an unprecedented research effort is being devoted to a form of radiation damage that is specific to fast reactors for, even though nuclear power, under pressure from environmentalists, is unfashionable, those persons responsible for national energy policy know perfectly well that in the long run most power must come from nuclear reactors, and the fast reactor in particular.

Radiation damage in fast reactors is a consequence of the fast neutrons and the high fuel temperatures: fuel swelling is caused by the formation of voids, which are themselves formed by the selective agglomeration of excess lattice vacancies resulting from neutron damage. When a neutron starts a collision sequence which causes a number of atoms to be knocked out of the crystal lattice, equal numbers of vacancies and interstitials result. If, as is all too apt to happen, the interstitial atoms migrate faster than the vacancies, then the former quickly disappear at "sinks" and the vacancies are left high and dry; they are then likely to combine to form microscopic cavities or voids, and the fuel or the material of the fuel envelope swells dangerously. This has been a serious problem, but because of extensive research since 1967 it is now well on the way to solution.

One of the principal remedies is to use alloys containing a fine dispersion of precipitates; migrating interstitials are in some way arrested when they impinge on a precipitate particle, and are held captive there until they are neutralized by a wandering vacancy. So, in the end, almost all the interstitials recombine with vacancies and few vacancies are left to form voids. Thus, some nickel-base alloys of the Nimonic type have been found particularly suitable for the manufacture of fuel cans, for the fine precipitates of γ' (ordered Ni_3Al) impede swelling in the manner described. For this purpose, it is necessary for the precipitates to be particularly finely distributed (to increase the probability of interstitial capture), and to stay that way in service. It is this last requirement which is difficult, because all precipitate populations are subject to the law of Ostwald ripening —that is, operation of the Matthew Principle, or the growth of the large at the expense of the small.

A group of investigators at Harwell have now systematically examined, both theoretically and experimentally, the behaviour of precipitate populations in a radiation field. The Matthew Principle is counteracted by the steady destruction of precipitates by neutron damage, and the diffusion of solute atoms into the matrix at a rate which is itself accelerated by the presence of excess vacancies. From their theoretical calculations, Nelson, Hudson and Mazey (*J. Nucl. Mater.*, **44**, 318; 1972) find that bigger particles redissolve faster than small ones, and that this is true whichever of two alternative mechanisms of resolution operates.

The final conclusion is that in the presence of steady neutron irradiation, large particles dissolve preferentially but small particles on balance still grow, so that a dynamic equilibrium is established and most particles finish up close to a preferred size, which is quite small. Irradiation thus effectively neutralizes Ostwald ripening. This conclusion is confirmed by experimental observations on a Nimonic-type alloy containing coherent γ' particles, but not by observations on another kind of nickel alloy containing incoherent precipitates. The last of these are subject to normal coarsening, because (it seems) one of the mechanisms for irradiation induced resolution of precipitates, which requires mass transport across the particle/matrix interface, does not work satisfactorily across incoherent (high energy) interfaces.

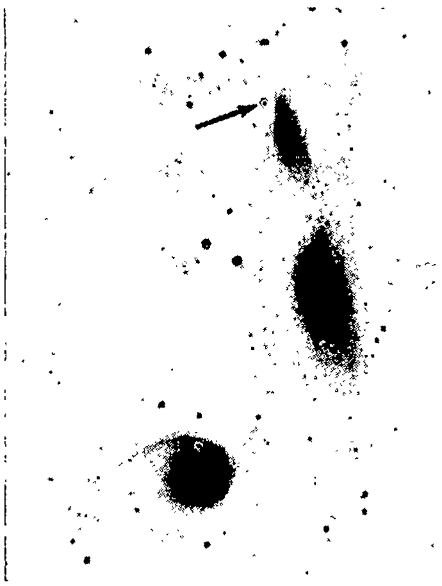
BL LAC OBJECTS

Link with Galaxies?

by our Cosmology Correspondent

BL Lacertae is the archetype of a class of interesting extragalactic objects. These BL Lac objects seem to be exceedingly compact, and are in many ways reminiscent of QSOs, with the important difference that they have no spectral lines and thus no measured redshifts. Although only half a dozen of the objects are known, and perhaps no more than three can be confidently said to be of the same family as BL Lac itself, they have recently been the subject of intensive study because they may be related to QSOs.

One interesting speculation—it is no more at present—is that BL Lac objects may be blueshifted QSOs; their flat, line-free spectra could well represent a region "normally" seen in the infrared. This idea is important, even though the sample of BL Lac objects is so small, because the definite detection of even one blueshifted QSO would have a significant bearing on the "redshift/distance relation" of QSOs. There is mounting evidence that the redshift of QSOs cannot be explained simply as a Doppler effect of motion in an expanding universe, and that part of the redshift, in some QSOs at least, must arise in some other way.


NGC 2993 (bottom), NGC 2992, and Weedman 2 (arrow). (Plate obtained by H. C. Arp.)

Paramount among the reasons underlying this view is the discovery of some

QSOs which seem to be physically associated with galaxies. In some such associations, the QSO has a redshift much larger than that of the galaxy with which it is associated, although such an association would imply that both objects are at essentially the same cosmological distance and should thus, on a simple cosmological model, be receding at the same velocity.

Interest in this situation is now heightened by the discovery of a blue stellar object which is probably a member of the BL Lac family and seems to be associated with the galaxy NGC 2992 (Burbidge *et al.*, *Astrophys. J. Lett.*, **178**, L43 ; 1972). NGC 2992 has already been noted as part of an unusual system ; Burbidge *et al.* reproduce the illustration from Arp's *Atlas of Peculiar Galaxies* (see figure) which shows the distortion of this galaxy and its neighbour NGC 2993, and the bridges of luminous material which not only seem to link the two galaxies but also extend in the direction of Weedman 2, a BL Lac type object. As Burbidge *et al.* point out, "If a physical connection could be established between Weedman 2 and NGC 2992, it would be of great importance in establishing the nature of the QSOs and/or the BL Lacertae type of object".

Like the other eight very blue stellar objects appearing near galaxies which were catalogued by Weedman (*Astrophys. Lett.*, **9**, 49 ; 1971), No. 2 was chosen because it is blue (the spectrum shows an ultraviolet excess), brighter than 19 mag on the blue plates of the Palomar Sky Survey, and close to a galaxy with a maximum diameter greater than 1 arc min. Weedman 2 is the only object which this search found near to one of Arp's peculiar galaxies ; it is also interesting that Weedman's criteria are so restrictive that many known QSOs would not qualify for selection under them.

Burbidge *et al.* have found that the continuous spectrum of Weedman 2 is very similar to that of many QSOs. Short of 6,000 Å, there is a slow rise towards higher frequency, roughly a power law with index ~ 0.3 ; at longer wavelengths there is a steep negative slope, index ~ -4. There are, however, no discrete spectral features. Weedman 2 is, then, a QSO without spectral lines, or a BL Lac object. Both the nearby galaxies are highly excited systems, showing strong emission in the Balmer lines, some oxygen lines, and other features. They have much the same redshift. Is Weedman 2 physically associated with NGC 2992?

If all three objects are at the distance implied by a straightforward cosmological interpretation of the galaxies' redshift, then the distance from Weedman 2 to the centre of NGC 2992 is only 22 kpc, roughly the same as the diameter of our Galaxy. There is no doubt that gaseous material could extend out to this distance from NGC 2992, and the luminous matter seen in the direction of Weedman 2 might well be being excited by radiation from that object to make it the prominent feature visible on the plates. The energy which Weedman 2 must be emitting, if at the distance implied by the redshift of NGC 2992, is 5×10^{42} erg s^{-1}, typical for a bright spiral and so both adequate to account for the radiation from the luminous bridge and small enough to be plausible.

GLACIATION

Argentinian Chronology

from our Geomagnetism Correspondent

ALTHOUGH the delineation of the geomagnetic polarity-time scale for the past few million years has played an important part in defining global concepts and processes, geologists and geophysicists have recognized for many years that in the longer term the scale should be no less useful in elucidating more local stratigraphic problems. This is likely to be the case particularly where radiometric dating is not possible or where precision in dating is difficult to achieve, although even where accurate radiometric dating is technically feasible the use of palaeomagnetic techniques may be quicker and cheaper, especially where there is some advantage to be gained from the study of many individual rock units. Even in cases where the statistical problem is less acute, however, there may still be some benefit in employing palaeomagnetism, whether or not independent radiometric ages are available.

A good example of the combined use of palaeomagnetic and radiometric dating is provided by a recent study of late Pliocene and early Pleistocene glaciation in southern Argentina, carried out by Fleck *et al.* (*Earth Planet. Sci. Lett.*, **16**, 15 ; 1972). The site investigated was on the Cerro del Fraile, a hill about 200 km south of Lago Argentina which comprises Cretaceous sediments capped unconformably on its western face by about 180 m of late Cainozoic basalt lava flows with interbedded glacial and fluvial deposits. The stratigraphic sequences studied by Fleck and his colleagues are more adequately represented pictorially but can simply be described as (starting at the base) cobbles–sand–1–A–cobbles–B–2–C–3–D–4–E (not sampled)–5–F–G–6–H, where the letters refer to basalt lava flows and the numbers to till layers.

Huntite makes a Brighter White

IN next Monday's *Nature Physical Science* (January 8), Veen and Arndt describe for the first time the occurrence in soils of the mineral huntite, $CaMg_3(CO_3)_4$. But huntite has an alias, pahn-jahn, and this makes their report of more than mineralogical interest alone.

Huntite was first described about twenty years ago from magnesian limestones in Nevada. Since then it has been found in evaporites along the Persian gulf and in secondary carbonate deposits in limestone areas. Now it has turned up in some Australian soils.

The soils in question are vertisols, or cracking clay soils, formed over basalts near Katherine, Northern Territory. Vertisols are almost exclusively found in those parts of the tropics with a marked dry season. Their name derives from the heaving of the soil layers, caused by the presence of clay minerals like montmorillonite which swell on wetting.

During the dry season there is an upward movement of moisture caused by evaporation losses from the ground surface. As the result of the concentration of dissolved salts by evaporation, carbonates, sulphates or chlorides of Ca, Mg, Na and K may be precipitated, the relative amounts of the various ions determining what minerals form.

In the case considered by Veen and Arndt, the dominant mineral would be expected to be dolomite, $CaMg(CO_3)_2$. But, perhaps because the basalts are rich in magnesium, huntite and aragonite (a variety of $CaCO_3$ not often found in soils) have formed instead. Veen and Arndt think that the explanation lies in the ability of small amounts of Mg ion to inhibit the formation of calcite layers, common to both dolomite and calcite crystals. The amount of Mg^{2+} present is, however, insufficient to allow the formation of magnesite ($MgCO_3$), and under these conditions the stable carbonates are huntite and aragonite.

Alias pahn-jahn, huntite powder is a white pigment which the Aborigines prefer to kaolin-based paint for personal and other decorative purposes. The reason for this preference, Veen and Arndt suggest, is the greater lustre and reflectivity of carbonates as compared with clay minerals generally. In the particular case of huntite, the effect may be enhanced by the occurrence of the mineral as minute but perfectly oriented crystals.

Assuming that awareness of the colouring properties of pahn-jahn dates from the distant past, one might infer that discovery honours for the mineral in soils should really go to the Aborigines. But at the very least, Veen and Arndt have now provided a chemical gloss for the term.

The whole sequence overlies the Cretaceous sediment.

Potassium-argon ages ranged from 2.06×10^6 yr for flow B to 1.03×10^6 yr for flow H, flow E not having been measured and the age of flow A being intermediate. All the flows (certainly B–H and probably A as well) were thus extruded during the Matuyama reversed geomagnetic epoch. But whereas flows A, D and G were reversely magnetized, flows B, C, F and H were normally magnetized. It is clear from these relationships, therefore, that three separate normal events within the Matuyama epoch had been sampled.

Specific radiometric ages (2.06×10^6 yr for flow B, 2.05×10^6 yr for C, 1.67×10^6 yr for F and 1.03×10^6 yr for H) suggest these to be the three known principal normal events—the Réunion, the Olduvai and the Jaramillo—although there are some small discrepancies between these results and previously accepted values. A new summary by Dalrymple (in *Calibration of Hominoid Evolution*, Scottish Academic Press, Edinburgh, in the press), for example, shows the split Réunion event to be represented by normal flows in the age ranges 1.95 to 2.01×10^6 yr and 2.08 to 2.09×10^6 yr. The ages of flows B and C could thus imply either that at least one of these ranges requires extension or that the Réunion event is really a triplet. Moreover, the Jaramillo event is usually said to have begun about 0.95×10^6 yr ago. The age of flow H thus implies either a Jaramillo event starting rather earlier than hitherto supposed or a split event. These small differences apart, however, it is clear that the Cerro del Fraile section includes all three principal normal events in the Matuyama epoch ; and in this respect it is unusual if not unique.

The existence of six till layers certainly indicates repeated glaciation and, assuming none of the lava flows to be subglacial, would seem to imply no less than six glacial events. Geological and petrological evidence previously adduced by Mercer (*Science*, **164**, 823 ; 1969), while not ruling out a subglacial origin for every single flow, nevertheless militates against such an origin. Thick baked zones cover several of the tills, for example, and no hyaloclastic material was detected in any of the samples examined petrologically. Moreover, the fact that individual flows cover a distance of up to 4 km suggests free flow over a gently sloping surface. Further evidence for at least one non-glacial period between glacial events represented by till is the existence of fluvial cobbles and gravel between flows A and B.

The age relationships between glacial and non-glacial periods are deduced by reference to the palaeomagnetic-radiometric time sequence. The earliest glaciation is represented by the till (1) beneath flow A. The age of flow A is not precisely known but the flow must be older than the 2.06×10^6 yr of flow B and, because it is reversely magnetized, presumably younger than the 2.43×10^6 yr age of the Matuyama-Gauss boundary. The second glaciation, which follows the ice-free period represented by the cobbles above A, is precisely dated by the till (2) which lies between the 2.06×10^6 yr-old flow B and the 2.05×10^6 yr-old flow C. The third glaciation (till 3) occurred less than 2.05×10^6 yr ago but earlier than the 1.86×10^6 yr represented by the non-subglacial flow D which indicates another ice-free period. The area was then glaciated twice (tills 4 and 5) between 1.86 and 1.67×10^6 yr ago and at least once (till 6) between 1.47 and 1.03×10^6 yr. There is no evidence of glaciation between flows F and G dated at 1.67 and 1.47×10^6 yr, respectively.

Finally, what, Fleck and his colleagues ask, are the climatic implications of these repeated glaciations? At present, the Cerro del Fraile, being in the rain shadow of the Cordillera, has no permanent ice cover. Nevertheless, if the landscape were less dissected between 1 and 2×10^6 yr ago, as it must have been, the Cordilleran ice could have covered the Cerro del Fraile even under climatic conditions similar to those of today. Certainly there seems to be no necessity to invoke lower temperatures to explain the repeated glaciation although, in view of the lack of information on ancient elevations, neither can lower temperatures be ruled out *a priori*.

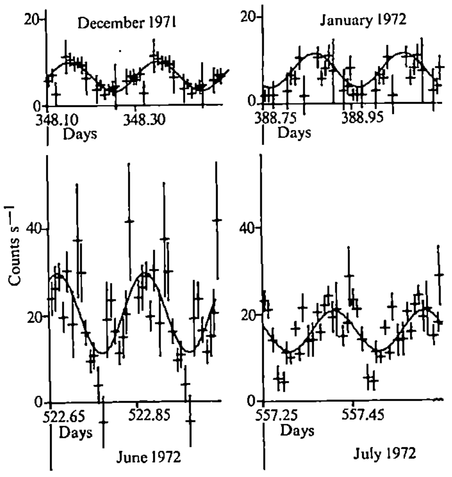
Unfortunately, as Fleck *et al.* point out, existing southern hemisphere palaeotemperature data (from marine strata now exposed on land or from microfossil and coarse-sediment content of deep sea cores) are not conclusive on this point because of disagreement between the workers involved. Nevertheless, Cerro del Fraile glaciations come to the closest agreement with the palaeotemperature scheme of Kennett *et al.* (*Science*, **171**, 276 ; 1971) who proposed coolings at 2.5×10^6 yr ago, between 2.13 and 2.10, between 1.98 and 1.88 and between 1.77 and 1.61×10^6 yr ago. Other schemes are also consistent with the Cerro del Fraile data, if less so ; but some—for example, the warmer climate between 1.8 and 1.6×10^6 yr suggested by Bandy *et al.* (in *Antarctic Oceanology*, **1**, American Geophysical Union, 1971)—are certainly not.

Variations of Cygnus X-3

By combining data obtained from three satellites, Canizares *et al.* have been able to deduce a very accurate period for the X-ray variation of Cyg X-3. This source has been observed by the Uhuru and Copernicus satellites, and both studies have revealed a variation in the X-ray flux with a period of approximately 4.8 h. Since the recent radio outbursts from the source (see *Nature Physical Science*, October 23, 1972) Cyg X-3 has been the subject of many searching investigations; in next Monday's *Nature Physical Science* (January 8) a team from MIT report observations made by OSO-7 in December 1971 and in January, June and July 1972. From these observations and those made by the two other satellites, a clearer picture of the behaviour of Cyg X-3 is now emerging.

The most notable feature, apart from the regular variation, is that the mean intensity of the source is not constant. Between December 1971 and June 1972, the mean changed by more than a factor of three. Also, the shape of the best-fit curve to the data points changed over a six month period, so that in the later observations the changes from maximum to minimum intensity are more abrupt than they were in December 1971 and January 1972. There are also variations in the intensity of Cyg X-3 and these show no regular pattern but occur on a timescale of tens of minutes, reminiscent of the variations seen in other discrete X-ray sources.

If the period of the source is assumed constant throughout the period of observation by the three satellites, which extends from December 1971 (OSO-7) to September 1972 (Copernicus), it is fitted best by a 0.199672± 0.000008 day variation. The OSO-7 data alone suggest a period of 0.199667 ±0.000014 day, and the Copernicus data alone give 0.1997±0.0004 day. Canizares *et al.* suggest that the data imply a period constant to 1 part in 1,500 over 7 months.



OSO-7 data for Cyg X-3 with best fit curves. Error bars show uncertainties of one sigma.

Monitoring Underground Explosions

DAVID DAVIES

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Seismological means for detecting and identifying underground nuclear explosions have improved steadily during the past ten years. A technique exists for separating explosions from earthquakes. The problem now is lowering the threshold and understanding the occasional problematic event.

An underground nuclear explosion converts about 1 per cent of its energy into seismic waves and these carry information about the time, size, and location of the event. They may also indicate that the event is indeed an explosion and not an earthquake. This information is somewhat more difficult to extract, and research in many countries for the past few years has been intensively directed towards discrimination between natural and artificial events. There is no other known way of identifying underground explosions that can be used on a world-wide basis. In this article, I shall describe the progress that has been made recently in this science, which has such obvious implications for arms control. The conclusions that I reach should not, however, be construed as a measure of the prospect of a total test ban. Many ingredients go into the making of a treaty, and ability to police it is only one of them. Seismological capability is thus not sufficient, but it may be necessary, at least down to some level of explosive yield. What would constitute an adequate level is a matter of some discussion at present. The science reported here is the result of the research of many seismologists. In order to reduce the number of references to a manageable level, however, I have cited only a few large compilations of results in which the genealogy of the various ideas and instruments may be found.

The reason for testing nuclear weapons underground is not, of course a matter of public discussion, but a paper by Neild and Ruina[1] probably provides a reasonably complete list of purposes. Between 1968 and 1971 there was an average of about twenty-five underground tests a year announced by the United States compared with about ten presumed tests a year for the Soviet Union, one test per year for China and about five a year for France—all but one of the Chinese tests and all of the French tests being atmospheric. Britain has not announced a test for seven years.

When the banning of nuclear tests first became an international issue in 1958, a conference on the technical problems in Geneva clearly indicated that the science of seismology would need substantial advances to reach a stage at which instrumental observations could indicate unambiguously that an explosion with a yield of a few kilotons (kton) had been detonated. Indeed the rather meagre data available during that conference and the subsequent negotiations (there had at that time only been two or three quite small underground tests) suggested that a first objective could reasonably be an international network of about 170 stations which could detect seismic signals down to a certain threshold but not necessarily identify their source. It was expected that most seismic events would clearly indicate their earthquake nature by their location and depth, their radiation pattern and the shape of their signal, but there would be a residue which would need further investigation. In the early days of international negotiations, inspections of the sites of a fraction of these suspicious events were discussed in detail—the number and nature of such inspections being particularly contentious topics. With time, the position of the Soviet Union on the inspection issue hardened to the assertion that inspections were unnecessary, and that purely national means of policing would be satisfactory. Thus the "Geneva network" was never built.

The two issues which were seen as central in 1958 are central today. Background seismic noise (from wind, traffic, ocean waves, and so on) placed a limitation on the detection of events; and a certain number of earthquakes did not immediately reveal themselves as such. The advances in seismology have been substantial since 1958, but increasing the signal-to-noise ratio (s.n.r.) and finding improved methods of separating earthquakes and explosions are still the principal fields of research. The rather narrow frequency bands involved in seismology have controlled techniques rigorously, and because the work is concentrated in situations of low s.n.r., the problem has been that of finding the frequency at which the s.n.r. is highest, and aiming improvement at that frequency, rather than trying to encompass the whole spectrum of the seismic signal. This "mission-oriented" approach to seismology, when combined with the intellectually stimulating problems that have arisen on the way, has exerted a vital role in the development of seismology since 1958.

It was clear from very early in the Geneva discussions (which lasted until 1962) that whatever international arrangement might finally develop, national interests required an improved seismic capability. The United States, Britain and Sweden, in particular, started to modernize their seismological capability for the explicit purpose of test-ban monitoring. Other countries, notably Canada and Japan, were also improving their seismic capability. The US programme "Vela Uniform" has been easily the largest, and so far more than $150 million has been spent on research and development. What has been bought?

Recording of Seismic Signals

In the first few years basic research was heavily supported and a network of 100 seismic stations, the World-Wide Standard Seismographic Network (WWSSN), was established—no stations were, however, sited on the territory of the Soviet Union or her allies. The network provided a huge data base, uniformly recorded, of short period (around 1 s) and long period (around 20 s) seismic signals.

Certain "realities" soon emerged from this work. The decreasing prospects of an international network with access to the Soviet Union led to the dominance of teleseismic studies; seismic body waves (P and S waves) are well registered up to a few degrees from the source; indifferently and variably from there to about 25°; and then clearly and predictably out to 100°. Distances are measured in central angle degrees. Some examples of P waves are given in Fig. 1. This last, teleseismic, zone covers half the world and would be crucial if access were not permitted to particular countries. The zone of observation having been restricted, immediate limits can be placed on the detectability of explosions. A 5 kton explosion in hard rock, such as granite or salt, produces in the teleseismic zone a P wave of amplitude around 5 nm at a period of 1 s. Background noise at 1 s is about a third of this figure for the best observatories. Thus in the absence of techniques for noise rejection, a network would usually detect a 5 kton explosion in hard rock (an event cannot be said to have been detected until recorded with a signal-to-noise ratio of at least 1.5 at four widely spaced stations). The capability declines drastically below this yield. Further, explosions in softer rocks, notably tuff, a volcanic ash common in Nevada, produce a smaller signal by a factor of at least two than comparable explosions in hard rocks. Explosions in dry alluvium have even smaller seismic effects—1 kton in hard rock and 10 kton in alluvium are roughly equivalent. There is, however, a limit to the thickness of dry alluvium to be found anywhere on Earth, and as an explosion has to be adequately buried for safety's sake, it is unlikely that explosions of more than about 20 kton can be fired and contained in known deposits of alluvium.

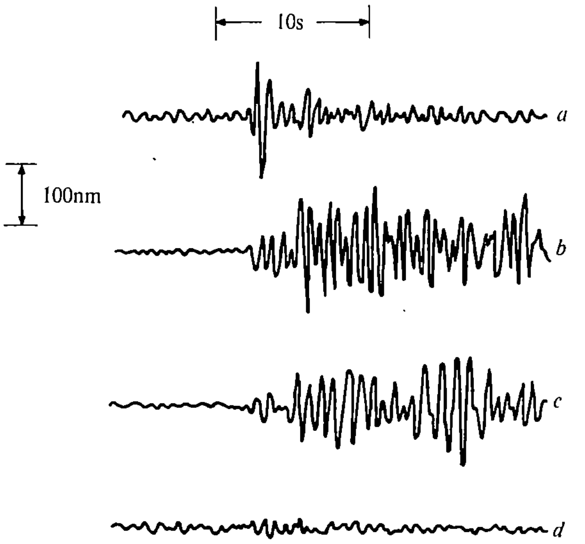

Fig. 1 Short period teleseismic observations of P waves from events located in *a*, Eastern Kazakh, USSR; *b*, Alaska; *c*, Turkey and *d*, South Sinkiang Province, China. The top and bottom events are presumed underground explosions. All events have body wave magnitudes in the range 5.0 to 5.7. Note the great difficulty there would be in identifying the direction of first motion for these events.

At the same time that the WWSSN was being equipped with conventional instruments and photographic recording, several experiments with arrays were being conducted. The aim was to suppress noise, presumed incoherent, by the addition of many channels. Another advantage accrued in the recording of data on analogue and later digital tape. Although practically all decisions in seismology are taken on the basis of observation by eye, direct visual recording suffers obvious disadvantages of dynamic range. Further, there is a strong noise peak at a period of about 6 s arising from microseisms generated in the oceans and the rejection of these by WWSSN instruments, peaked at 1 s and 20 s, is usually not entirely satisfactory. As a result, film records, in which the magnification is controlled by the ease of viewing, are often dominated by 6 s microseisms and are thus not running at the best magnification for 1 or 20 s signals. The data processing possibilities of tape recording remove this obstacle.

The first arrays built in the United States had an aperture of 4 km. They were in many ways prototypes of possible arrays that the Geneva meetings had envisaged for an international network. Up to sixteen seismometers were spread out over this aperture, and the signals from all seismometers were added without phasing. Seismic signals from teleseismic distances arrive at steep angles—the signal sweeps across the ground with a horizontal phase velocity of at least 10 km s^{-1} and up to 24 km s^{-1}, and at typical sites this corresponds to angles of incidence of less than 20°. Thus straight addition does not seriously degrade the 1 s component of a signal seen in the small aperture. It was found with these small arrays that the noise was coherent in this frequency band for distances typically greater than the 0.5 km spacing of instruments, so the gain in s.n.r. was somewhere between one (if the noise were totally coherent and travelling in a near vertical direction) and $\sqrt{N}$ (if the noise were totally incoherent). Later arrays have used a seismometer spacing of around 2 km, at which distance local noise is substantially incoherent.

The next development was the medium aperture phased array implemented by the United Kingdom Atomic Energy Authority[2]. Up to twenty seismometers were laid out in two perpendicular lines. Arrays of this type are in operation in Canada, Brazil, Scotland, India and Australia. The aperture was large enough to require phasing of the signal after recording to steer the array in the appropriate direction, but small enough to ensure that the signal was still coherent. Signal-to-noise improvements approaching $\sqrt{N}$ (about 4.5) are obtainable.

The first large aperture seismic array (LASA in Montana) was completed by the United States in 1965, and a second array (NORSAR in Norway) has been in operation about two years. LASA has an aperture of 200 km and 350 short period seismometers; NORSAR is somewhat smaller. LASA is steered (by a computer) to be face-on to incoming seismic signals and the angle of approach is sufficiently well determined to locate the source with an accuracy of one or two hundred km. The real time digital operations of LASA and NORSAR each occupy entirely two medium sized computers in hunting for P waves. The gain for large arrays does not meet the $\sqrt{N}$ expectation, however, for over an aperture of 200 km crustal geological conditions can vary widely and this leads to a degrading of the coherence of the signal. An improvement in s.n.r. of a factor of ten is possible for LASA, however, and the array is capable of detecting and locating explosions in the teleseismic zone with yields down to about 2 kton in hard rock. Several thousand earthquakes occur each year with P waves of comparable or greater amplitude, and these form the population against which explosions have to be discriminated.

It became increasingly apparent in the mid 1960s that the registration of body waves was not sufficient to solve the discrimination problem; a broader spectrum of seismic data was necessary. The answer lay in the dominant signal on the long period seismic traces, the Rayleigh wave. This is a dispersed wave which has travelled over the Earth's surface and is well excited at 20 s periods—there are short period Rayleigh waves and long period P waves, but they are unimportant for discrimination. As for short period recording, noise is the limiting factor. The 6 s oceanic microseismic background, longer period fluctuations arising from atmospheric effects and the interference of Rayleigh wave trains from other earthquakes all contribute to the background. In the absence of an interfering event, most seismic stations have a background noise level at 20 s period of 50 to 100 nm; there is a great variability in noise level both from place to place and in time. For the reasons already given, tape recording is most desirable.

Rayleigh waves spread cylindrically, but also undergo other attenuation in the ground. The signal decays as distance (Δ) to the power 1.6. This rapid decay makes it imperative that the seismic station be sited as near to the event as possible. Within a political requirement of non-intrusive monitoring we have to consider a value of Δ of 20° as the minimum at which stations will be available. At 20°, the Rayleigh waves from a 10 kton explosion with 20 s period are somewhat less than 100 nm in amplitude, so individual stations at this distance have a relatively small probability of detecting surface waves. As with short period observations, arrays prove a valuable means of increasing the s.n.r. Instrument spacings have to be greater (typically 20 km) for noise to be incoherent. Small tripartite arrays are either under construction or recently completed in Sweden, Canada and India. LASA, NORSAR and ALPA (an exclusively long period array in Alaska) all have at least fifteen long period seismometers within them. Results from LASA indicate an improvement in s.n.r. of a factor of four—close to $\surd N$. In addition, knowledge of the nature of the dispersed waveform allows matched filter techniques to be applied, and these contribute up to another factor of two to the signal-to-noise ratio. Thus a twenty element long period array can yield an order of magnitude improvement in the s.n.r. against incoherent noise. In addition an array has a certain amount of directional discrimination (Rayleigh waves have a wavelength of 80 km at 20 s period) which makes it possible to study an event in the presence of an interfering signal, provided that the two are coming from directions differing by more than 30° and that the interfering signal is no more than a factor of ten larger than the signal being studied.

Recent developments in instrumentation have been successfully aimed at reducing the non-seismic noise in instruments by more effectively sealing and isolating them, and at broadening their response to cover a wide spectrum. There is also promise in the siting of instruments down boreholes where long period noise is frequently substantially lower.

Seismic Magnitude

Both P waves and Rayleigh waves are used to define a magnitude for seismic events. The body wave magnitude (m_b) on the Richter scale is a measure of the excitation of P waves. The amplitude of the P wave signal on the record is converted to ground displacement (A) at a dominant period T, and then used in a formula

$$m_b = \log_{10}\frac{A}{T} + B(\Delta)$$

where $B(\Delta)$ is a term counteracting the variation of the signal with distance from the source. A ground displacement of 10 nm at 1 s period at a distance of 60° from a source indicates an event of magnitude 4.7, for example.

The surface wave magnitude is obtained by measuring on the Rayleigh wave the ground displacement A at a period T (usually near 20 s) and using a formula

$$M_s = \log_{10}\frac{A}{T} + 1.66\log_{10}\Delta + 0.3$$

An event with an M_s of 4.0 will have a ground displacement at 30° of 300 nm at 20 s period.

For earthquakes, there is an empirical and very scattered relationship between M_s and m_b, the best fit to which is

$$M_s = 1.59m_b - 3.9$$

I shall discuss this relation further later.

It is possible to relate both m_b and M_s to the yield for explosions. Two kton in hard rock produces an event with an m_b of 4.0, 20 kton an event with an m_b of 5.0. For higher yields the equivalence of a factor of 10 in yield to a change of one unit in magnitude breaks down for several reasons. I have already noted that softer rocks produce smaller seismic signals; an m_b of 4.0 is equivalent to 2 kton in granite, 3 or 4 kton in tuff and 20 kton in alluvium.

The surface wave magnitude M_s can equally well be related to the yield, and is a more useful measure, for it seems to obey a relation (for hard rock) of the form

$$M_s = 1.3\log_{10}Y + 1.5$$

over a range from at least 1 kton to 1 mton.

Discrimination

In the early development of the subject, the concentration on the detection of events by means of P waves led to a hope that the study of P waves alone might show differences between explosions and earthquakes. It was soon found that such differences did exist, but not to the extent that all earthquakes could be separated from all explosions; it was only possible to quote probabilities. Diagnostic aids, as they have come to be called, are the location and depth of the event, the direction of first motion of the seismic trace and the complexity of the signal. Clearly if an event can be unequivocally identified as having occurred deeper than a few km it is not an explosion—likewise if it occurs under deep water. The quality of depth determination declines as the depth decreases and it is frequently impossible to assign depths to events shallower than 30 km. The first motion criterion uses the difference in radiation pattern between a totally compressive explosion and an earthquake for which the radiation is successively compressive and rarefactional in adjacent quadrants. There are numerous problems—the uneven distribution of stations around the globe and the high signal-to-noise ratio required to make polarity measurements both render the technique of little use for lower yields. "Complexity", a measure of the duration of the P wave signal, is a criterion which showed promise: signals that last more than a few seconds are likely to have come from earthquakes. Unfortunately there are many earthquakes which last for less than a second and these must be placed in the category of "suspicious events".

More recent work on the spectra of P waves has shown that even explosions of very small magnitude are significantly richer in high frequencies (2 to 3 Hz) than are earthquakes. This accords with generally accepted ideas of the nature of earthquake and explosion sources. Regional variations present problems, however; it seems at present that the attenuation (and hence the frequency transmission characteristics) of the Upper Mantle varies sufficiently from place to place that genuine spectral differences between earthquakes and explosions are overprinted with the frequency absorption of the Upper Mantle in such a way that P waves from explosions can occasionally look like those from an earthquake.

The broadening of the spectrum that the joint study of Rayleigh and P waves brought with it provided the one indubitable "breakthrough" that the subject has seen. It had been realized for several years that explosions did not generate anything like the amount of Rayleigh waves that did earthquakes of comparable body wave magnitude. The WWSSN allowed these observations to be put on a more quantitative and global basis. It was noted that if the

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surface wave magnitude M_s for each event was plotted against its body wave magnitude m_b, the natural and man-made events clustered round two well separated lines.

A typical example is shown in Fig. 2. Clearly the earthquake population has a wider scatter than the explosion population, and this is unsurprising considering the diversity of earthquake types. Vagaries of propagation in the real Earth also contribute to the scatter. Nevertheless one point can be asserted—that the diagram has greatly increased our confidence in identifying events above a certain size. Of course the purist may reasonably object that a diagram such as Fig. 2 cannot offer certainty as it is only a modest sized population; nevertheless the diagram has been widely accepted.

Earthquakes and explosions generate other seismic phases—shear or S waves and horizontally polarized surface waves called Love waves. In addition P waves have a long period component. All of these offer possibilities for discrimination, particularly because explosions in theory generate few S and Love waves. For large explosions and earthquakes, use of these waves works well, but it is found in general that the largest wave amplitude on the long period record is that of the Rayleigh wave.

$M_s : m_b$ Discriminant

Fig. 2 is taken from a recent study[3] using WWSSN instruments only. Each point represents one event in Eurasia and it is necessary to have P wave detections at at least four widely separated stations before an event is listed. This places a lower limit on the body-wave magnitude for which events are reported. There are several reasons why this threshold should be rather blurred, but as a gross simplification one can say that the global network of seismometers (excluding arrays) will detect by P waves at four or more stations almost all events with an m_b of 5.0 and greater and almost no events with m_b less than 4.0.

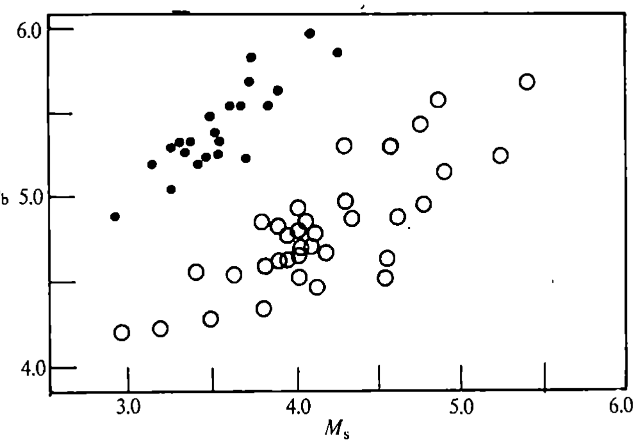

Fig. 2 An M_s : m_b diagram for Eurasia based on WWSSN recordings by Marshall and Basham. ○, Earthquakes; ●, presumed explosions.

Each point also represents a determination of surface wave magnitude, and it is customary to require at least four stations to have detected the surface wave before a value is accepted (this is a very crude way of allowing for the radiation pattern of earthquakes). An event with an M_s of 4.0 is certain to be detected by its Rayleigh waves, but an event with an M_s of 3.0 is unlikely to be detected. This is partially a statement about noise, but the locations of the receivers are also important as they need to be as close to the event as possible.

The thresholds of detection are such that an earthquake is likely to be seen both by its P and Rayleigh waves or by neither. This means that there are few earthquakes which are assigned an m_b but cannot be placed on the diagram because M_s is not measurable. On the other hand, there may be explosions which have, for instance, an m_b of 4.5 and (by extrapolation) an M_s of 2.5. If it is required that an event may be identified only if both parameters can be determined one can thus talk about a threshold for discrimination as the Rayleigh wave detection threshold. This threshold is statistical in nature, but may be defined in some such way as "If an event detected by P waves has an M_s of 3.2 or greater there is a 90 per cent chance that its surface waves will be detected at four or more stations and thus that it can be categorized as an explosion or earthquake". This somewhat portly statement is necessary because events are routinely detected by body waves but the crucial detection for discrimination purposes is of surface waves. An alternative version is "Explosions in hard rock of 20 kton or more can be identified as such; so can practically all earthquakes detected by the WWSSN".

It is obvious from Fig. 2 that any attempt to lower the yield threshold should reasonably start from an attempt to improve the detection of the surface waves, for it is demonstrable that there are events in Russia with an m_b of less than 5.0 which have no surface waves visible on present instruments but which may be presumed to be explosions. Obviously as a programme for improvement of surface wave capability developed it would be highly desirable to boost up body wave detection in order that almost all events with m_b greater than 4.0 be reported. Such a strategy is discussed later.

Science of Discrimination

Fig. 2 clearly indicates a difference in excitation between 20 s Rayleigh waves and 1 s P waves for the two types of event. A natural question is how this difference arises, and the question is not purely academic, because in attempting to lower the threshold (that is to bring in points with lower M_s and m_b) it is valuable to know exactly when the two populations merge. In Fig. 2 there is a clear separation, but least squares straight lines may not be the best representations of the relationships at lower magnitudes. Theoretical models for earthquakes and explosions should be extendable to any magnitude and thus should indicate whether capital investment to improve detection capability would be justified.

Unfortunately knowledge of the nature of both types of event is still shadowy. An earthquake is known to be a propagating rupture on a fault plane that leads to a finite offset across the fault; and an explosion as seen by seismometers is equivalent to the sudden application of an elastic stress on a notional surface of radius less than 1 km. It is also known in part how P waves and Rayleigh waves are generated from both types of source. This turns out not to be sufficient to answer the question of why the discriminant works. The question can be subdivided by recognizing that the discriminant may depend on the different partitioning of energy at source into body and surface waves; or differences in spectra at source that are reflected in differences in excitation at 1 and 20 s periods regardless of wave type; or some combination of these two.

I do not believe that we yet have a simple answer to this issue. This reflects the inability as yet to describe satisfactorily the processes at work at the focus of an earthquake. I think it is reasonable to say that it is not a depth dependence nor a size difference that controls discriminative capability. Beyond this it is difficult to go.

A more direct and at present more successful approach to the problem of the smaller magnitude events which are as yet beyond the global network's accessibility is to do pilot work in a region where there is the opportunity to get close in to events. Accordingly much research has been concentrated on observations of explosions at the Nevada test site and earthquakes in the western United States. Results have been reported by Evernden[4] and, even using standard definitions of M_s and m_b, separation is good down to the lowest yields observed. When careful allowance is made for regional propagation effects separation can probably be improved.

These results show that, within the context of relatively unrestricted access to the area, explosions and earthquakes in the western United States can be discriminated to substantially lower levels than the global threshold of 20 kton in hard rock. There seems to be an order of magnitude of improvement possible without encountering insuperable problems of overlap. It is of the utmost importance that this be understood in context. Monitoring of the Soviet Union, for instance, would involve forgoing the nearby stations and attempting to make up for the loss by high grade instrumentation, arrays and digital processing. Further, there is no guarantee that earthquakes and seismic wave propagation in the Soviet Union are comparable to those in the western United States (although there are grounds for optimism). Lowering the threshold of the monitoring network could, however, reasonably be expected to yield a lower discrimination threshold, and a large investment in such an improvement would be justifiable on scientific grounds.

The Future

Several instrumental developments and deployments are under way at the moment. A small number of high quality, long period seismometers are now set up (in Spain, Israel, Thailand, Australia, Alaska and New Jersey). Others, suitable for deep boreholes where noise may be substantially reduced, are in production. Two large new long period arrays, in Alaska and Norway, and three three-element long period arrays in Canada, Sweden, and India, are now operating. The hope is that within two years there will be sufficient data from these instruments to assess a new level of discrimination. It seems reasonable to expect at least a diminution of a factor of two, to 10 kton in hard rock, on the basis of these investments. This is equivalent to saying that in monitoring the Soviet Union almost all events with an M_s of 2.8 or greater will show detectable surface waves at four or more widely spaced stations. As a goal this is quite modest; the two large arrays plus the new stations in Thailand and Israel alone should accomplish this.

A considerably lower threshold seems, however, to be attainable. Extrapolations from the western United States suggest that it is not at all unreasonable to expect discrimination to be feasible at an M_s of 2.0 (2 to 3 kton in hard rock). How would this be achieved? If a monitoring network is allowed the luxury of expanding, the country being monitored must be allowed the luxury of moving its test-site to the most remote spot possible. It would be possible for the Soviet Union to test at a distance of 30° from the nearest seismometers in a monitoring network, and, at this distance, surface waves from an explosion with an M_s of 2.0 are less than 10 nm peak to peak. There are few stations with a noise level as little as a factor of ten higher than this; and a factor of ten might be the upper bound on what the largest possible array might contribute to the improvement of signal-to-noise ratios.

At this stage, economics may control the threshold more than seismology. For instance, Professor J. N. Brune of the University of California, San Diego, recently estimated that a thorough programme to upgrade seismic capabilities to such a high level would cost at least $200 million.

How might a major programme reasonably develop? The present operation of WWSSN is decidedly non-optimal, as the network was not designed for, nor is it dedicated to, discrimination. Resiting of some seismometers, particularly removal from centres of population, would yield reduced noise levels. Better protection from environmental changes, particularly pressure and temperature fluctuation, could not but be beneficial. The aim should be to record ground noise only, and it is worth a substantial amount of time and money to ensure that this is all that is coming out of the instruments. Placing some instruments down boreholes could certainly reduce noise further. Digital recording, in parallel with photographic recording, is highly desirable, preferably with prefiltering to eliminate 6 s microseisms.

At present the WWSSN produces data, but no one is required to analyse them. A small group of seismic analysts, having available both the superior data and also information from the large arrays and other seismic stations that cared to contribute, would greatly increase our number of body-wave detections of events and would develop knowledge about which stations were most useful both in body and surface wave observations. This knowledge would help decide what the next step should be.

It is likely that certain stations would be worth even further improvement. Spotting these sites involves more than just measuring the noise. Seismology is not a wholly predictable subject and, in some locations, signals are unusually high for little known reasons. This may work in favour of sites which would be rejected on the grounds of noise level alone. The improvement might take the form of development of arrays centred on good stations. The establishment of new stations in favourable locations would also make sense.

Beyond this stage it is not easy to speculate. Once one has started reinstrumenting the globe there is no limit to the ingenuity that could be employed. Political and economic realities, however, restrain the monitoring network from extending too far. The development sketched out might be accomplished within five years.

Obstacles

The relative simplicity of Fig. 2 may give the impression that discrimination can be made into a list of instructions for seismic record readers. In most cases this is true, but there are nagging problems—some natural and some man-made.

In considering a population of events in a certain region it turns out that some events cannot be categorized on the basis of an $M_s:m_b$ discrimination because the surface waves from them are masked by surface waves from other unrelated earthquakes. These cannot be discriminated by the $M_s:m_b$ technique unless a way can be found to separate the two events. An array is highly desirable for this, and even then there are prospects of success only under the circumstances discussed earlier. If the masking event is very large (with an m_b of 7.5 or greater) the global network is blotted out to such an extent that detection of even P waves from practically any event for an hour or more afterwards may be impossible because of the reverberations within the Earth. This opens up the possibility for evasion by firing an explosion immediately after a large earthquake. It is difficult at present to see any seismic means of improving the prospect of detecting such evasions.

Another natural hazard is that of explosion-like earthquakes. If the time interval for which Fig. 2 had been compiled were expanded, earthquakes of quite high magnitude (an m_b of 5.0 for instance) but which produce barely discernible surface waves would eventually be found. These earthquakes, which come from very limited regions on the Earth's surface, would have to be classed as explosions according to the $M_s:m_b$ criterion. It is believed that they can be understood in terms of earthquakes in which the stress drop is abnormally high. Whether with improved instrumentation any earthquake-like features of these events will reveal themselves remains to be seen. It is not yet known whether, with improved body wave detection capability and hence larger populations of smaller events, more of these earthquakes would be encountered.

The chief man-made problem (apart from deliberate masking by earthquakes) is that of decoupling. The radiated seismic signal from an explosion fired in a sufficiently large hole can be at least a factor of 100 smaller than in the fully tamped case. Thus a 50 kton explosion could be moved below the bounds of detectability if fired in a deep hole of radius 80 m, and partial decoupling would occur if the radius were less than this. Although a removal enterprise of this magnitude might well excite attention if started after a treaty had been signed, there may at present be cavities in salt mines which could be used for partial decoupling. There seems no seismic way of detecting decoupled events, and entrants into a treaty would have to weigh the risks accordingly.

Although there are prospects of reducing the yield threshold to a figure of a few kton in hard rock, it must be borne in mind that a violator is unlikely to fire his explosions in granite. As a threshold of 2 kton in hard rock would be very difficult to achieve, this might be turned into a statement that all tests under 20 kton fired in alluvium would not be discriminable. This depressing situation is fortunately unlikely to be valid. The thickness of alluvium deposits limits the depth of the shot, but, on the other hand, the shot must be buried deep enough not to form a subsidence crater. These craters have formed more often than not after a test in alluvium, and there would be a clear risk of visual detection. Thus a violator would have to judge the risks of alluvium firing and might well conclude that a yield much smaller than 20 kton was all that could safely be tested.

"Negative Evidence"

One may justifiably feel vaguely uneasy about the $M_s:m_b$ discrimination technique. It tends to enshrine a lot of science and technology in one diagram and it may be used misleadingly. For instance although the population of earthquakes in Fig. 2 is fairly representative, there can only be a limited number of explosions; most of these come from one test site and are thus not truly independent samples. Further, test sites could be moved around at will, and so the discriminant can only represent the past, not the future. These qualms can only be assuaged if the science of discrimination is seen to be well founded.

On the other hand, there may also be some uneasiness that the $M_s:m_b$ discriminant is not optimistic enough, and this is worth examining. When an event has both detectable P waves and detectable Rayleigh waves it can be placed on an $M_s:m_b$ diagram. If, however, P waves are detected but no Rayleigh waves are seen, it is unacceptable. For instance, an explosion in the Soviet Union with an m_b of 4.5 will not generate detectable Rayleigh waves. Could it be called an explosion on the basis of its lack of Rayleigh waves? Obviously this question depends on whether all earthquakes with an m_b of 4.5 have detectable Rayleigh waves (we eliminate the masked event problem). The answer is that on present experience they do, with the exception of a limited number of events mentioned earlier. The spread of M_s values for earthquakes with $m_b>4.5$ is substantial, but it does not extend down to 3.2.

Up to the present so called "negative evidence" has always been looked on with some suspicion. The reason for this is probably that, although to a scientist the absence of a signal can be as important as its presence, to the politician with a different mode of thinking "negative evidence" sounds as unconvincing as would absence of fingerprints to establish not being present at the scene of a crime. It may well be that the $M_s:m_b$ diagram, for all its neatness, has placed an undue emphasis on the necessity for determining both M_s and m_b.

The following would be a "negative evidence" type of discrimination statement. "When an event has been detected by P waves and assigned a body wave magnitude of 4.5 or greater it can be categorized as an earthquake if $M_s \geq (m_b - 1.3)$ and an explosion if $M_s < (m_b - 1.3)$ or if M_s cannot be determined, but on the basis of noise observations must be less than $m_b - 1.3$". It would switch the threshold to a body wave magnitude of 4.5 or about 5 kton in hard rock, a figure that with the $M_s:m_b$ discriminant alone would take several years and much expenditure to achieve. Although this statement would let through as explosions those unusual earthquakes described previously, this would equally apply to the $M_s:m_b$ technique. For these events a pragmatic approach is necessary. A very detailed survey with a large population is necessary to establish the general validity of negative evidence. Such work is at present being pursued.

The Broader Scene

I shall conclude with a description of recent activity beyond the laboratory. In 1968 the Stockholm International Peace Research Institute (SIPRI) convened a conference of seismologists from ten countries, east and west, at which technical progress since 1958 was reviewed. Subsequent SIPRI Progress Reports, the latest dated September 1971 (ref. 5), have kept the technical content up to date.

In the United States, numerous technical meetings have been held. Papers presented at the Woods Hole meeting in 1970 (ref. 4) have been widely used in this discussion. A recent meeting in Cambridge, Massachusetts, has allowed some of the projections to be strengthened and a growing appreciation of the problem events.

The Conference of the Committee on Disarmament of the United Nations (which has lived under several names) meets regularly at Geneva, and the issue of seismology and a test ban is frequently aired there. In 1970, at Canadian instigation, a register of seismic stations with guaranteed available data was compiled by the United Nations and subsequently a Canadian survey[6] examined the theoretical potential of this network. In the same year Britain submitted a proposal[7] to Geneva on a new network which would improve discriminative capability. In 1971 a United Nations technical meeting was held in Geneva against a background of increased international interest in a test ban.

It is clear that this subject will continue to remain alive before a more general public for the foreseeable future. During this time seismological advances are unlikely to be spectacular, but a continuing investment in seismology will undoubtedly produce a steady reduction of the threshold. Where this threshold ultimately comes to rest and whether a treaty will be signed will be determined by a multiplicity of factors, only one of which is seismology.

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Fig. 2 was kindly supplied by P. W. Basham and P. D. Marshall, and represents work done by them[3] at the Department of Energy, Mines and Resources, Ottawa, Canada.

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Diachronous Deposits: a Kinematic Interpretation of the Post Jurassic Sedimentary Sequence on the Pacific Plate

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We have constructed a kinematic model which outlines the deposition of the units of the western Pacific seafloor on growing crust. The average northward component of motion for the Pacific plate has been 4.4 cm yr^{-1} from 100 to 30 m.y. BP and 2 cm yr^{-1} from 30 m.y. BP to the present.

BENEATH the thin (20 to 100 m) unlithified layer of brown clay on the floor of the western Pacific abyss is a thicker (300 m) sequence of chalk, chert and clay, and the boundary between the two layers is broadly time transgressive, varying in age from Early Cretaceous in the west to Late Cainozoic in the east. Because there has been a tendency to attribute a precise synchroneity to pelagic facies, this evidence of widespread and apparently systematic diachronism is significant. Evidence of the time transgressive nature of pelagic deposits has been accumulating since the beginning of the deep sea drilling product[1-3], and during Glomar Challenger's Leg XX we extended observations of this phenomenon to the oldest known areas of the Pacific crust[4,5]. We have now also a kinematic model of pelagic deposition for the time transgressive sedimentary sequences of the Pacific basin, which may be applied to the stratigraphic succession on any oceanic plate.

A Mid-Latitude Model for Deep-sea Pelagic Deposition

There are at least three principal sources of deep-sea pelagic sediments—the remains of living organisms, terrigenous detritus supplied as wind blown dust or suspended matter, and pyroclastic material. The biogenic remains are composed predominantly of calcareous and siliceous tests which dissolve as they sink to and rest on the ocean floor. The solution of the tests is controlled by a number of variables which result in effective compensation depths below which no calcareous or siliceous remains are found[6,7]. Thus the record of biogenic sedimentation on the ocean floor will depend on the depth relative to the appropriate compensation depth. By contrast the inorganic component may be found at all depths. Other variables such as plate motion and crustal subsidence are thus only important because they control the location of the plate relative to sources of supply, the pattern of oceanic circulation and depth relative to the compensation depths.

We propose that as new oceanic crust is formed in the rift valley of the Mid-Oceanic Ridge a blanket of light-coloured carbonate ooze is deposited on the new crust until the subsiding sea floor drops below the carbonate compensation depth. Subsequently a blanket of slowly accumulating abyssal clay covers the organic debris (Fig. 1).

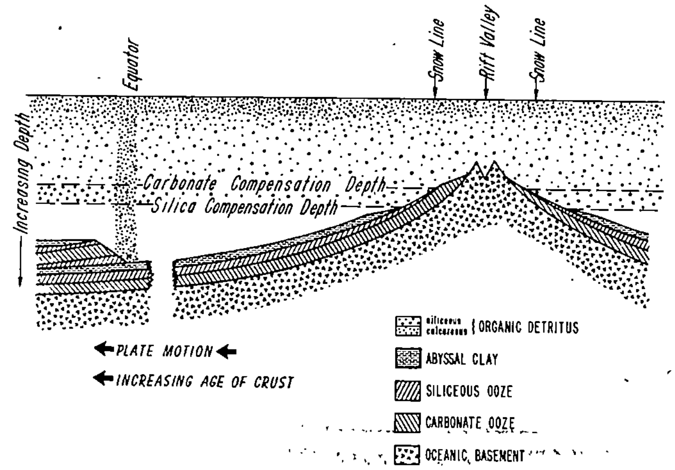

Fig. 1 Axially accreting model of oceanic sedimentation.

The thickness and nature of the biogenic debris are determined by the depth difference between the compensation depth and the initial depth at the ridge crest, the rate of subsidence, and the type of biogenic sediments accumulating at any particular latitude. In general, the compensation depth lies about 1,000 m below the ridge crest, and new crust subsides about 50 m (m.y.)$^{-1}$, allowing 20 m.y. of biogenic deposition before the onset of abyssal clay sedimentation. Sedimentation rates for pelagic biogenic oozes are less than 10 m (m.y.)$^{-1}$. Thus the basal calcareous layers can normally be expected not to exceed 200 m in thickness. Sedimentation rates for abyssal clay are generally significantly less than 1 m (m.y.)$^{-1}$. Thus Early Cretaceous (120 m.y.) crust formed under ideal conditions should have accumulated some 300 m of sediments consisting of 200 m of basal chalk and 100 m of overlying abyssal clay. Because the floor of the western Pacific is at least Early Cretaceous in age[3-5] we may compare the drilling results with the simple model.

Sediment Sequences in the Western Pacific

The sea floor of the western Pacific is covered by 5 stratigraphic units: a wedge shaped layer of Quaternary to Late Tertiary silty clay primarily of volcanic origin, thinning away from the Asiatic volcanic-arc source; a ~100 m thick layer of Tertiary to Cretaceous abyssal zeolitic clay; a sequence (±100 m) of Tertiary to Cretaceous cherts and chalks; an inferred earlier, thin abyssal clay a few tens of metres thick; and basal chalks, cherts, limestones and marls of Cretaceous age over 200 m thick (Fig. 2). Variations of this stratigraphy are seen in the Caroline Abyssal Plain, where Late Tertiary abyssal clays are intercalated with turbiditic calcareous oozes[4,5].

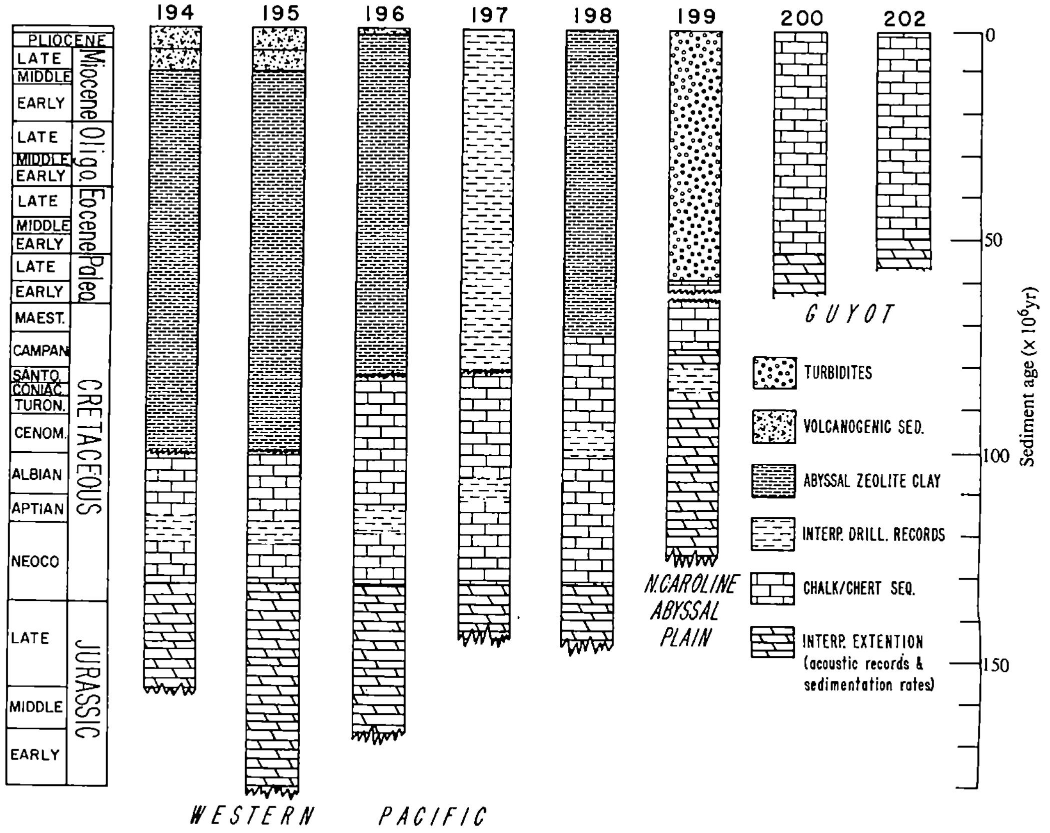

Fig. 2 Stratigraphic summary of Leg XX drilling.

An Initial Comparison

The stratigraphic history may in part be explained as the normal sedimentary sequence expected to overlie a section of axially accreting mid-latitude oceanic crust. But the comparison of the mid-latitude model with the stratigraphic sequence drilled during Leg XX reveals serious discrepancies. Not only are the two chert/chalk sequences together nearly twice as thick as predicted but the span of time from the first chalk to the last chalk is closer to 50 m.y. than the 20 m.y. given by the model. The simple model outlined applies specifically to the mid-latitudes and the mid-ocean, and may be modified by considering additional sources of sediments.

Equatorial Model

Anomalously high surface productivity may be expected to push the compensation levels ("chalk line") to much greater depths (Fig. 1) and may increase significantly rates of biogenic accumulation[8]. The most notable example of chalk-line depression occurs in a narrow zone between the northern hemisphere and southern hemisphere current systems, beneath the narrow zone of equatorial upwelling. Crust that forms under the equator may accumulate a considerable thickness of biogenic sediments. The specific thickness of sediments will depend on the rate and direction of crustal drift and the age of the crust at the time of equatorial passage[9,10]. Crust drifting parallel to the equator may accumulate enormous thicknesses, particularly on young crust, but crust drifting north or south receives a thinner chalk whose thickness depends largely on the rate of drift.

A belt of siliceous ooze deposition lies between the equatorial zone of mainly carbonate deposition and the vast expanse of barren abyssal brown clay which floors the deep Pacific. The belt of siliceous oozes, at the margins of the Equatorial belt of high productivity, may be explained by the greater effective silica compensation depth, and allows us to predict the presence of siliceous units above and below ancient equatorial carbonates (Fig. 1). The resulting diachronous deposits of siliceous sediments would seem to be likely candidates for diagenetic conversion to bedded chert. Because the borders of the equatorial belts of carbonate and siliceous ooze are known to have suffered extensive fluctuations in the Quaternary, we may assume that alternation of thin siliceous and thicker carbonate oozes is an overall characteristic of equatorial deposition.

In practice there seems to be a depth below which the chalk line may not be depressed. At present this depth lies near 5,000 m. Ocean depth is a function of crustal age; a depth of 5,000 m generally corresponds to crust more than 50 m.y. old. Thus crust older than 50 m.y. at the time of equatorial transit might be deprived of an equatorial deposit, or the transit may be represented by siliceous deposits or by a thin sequence of carbonates.

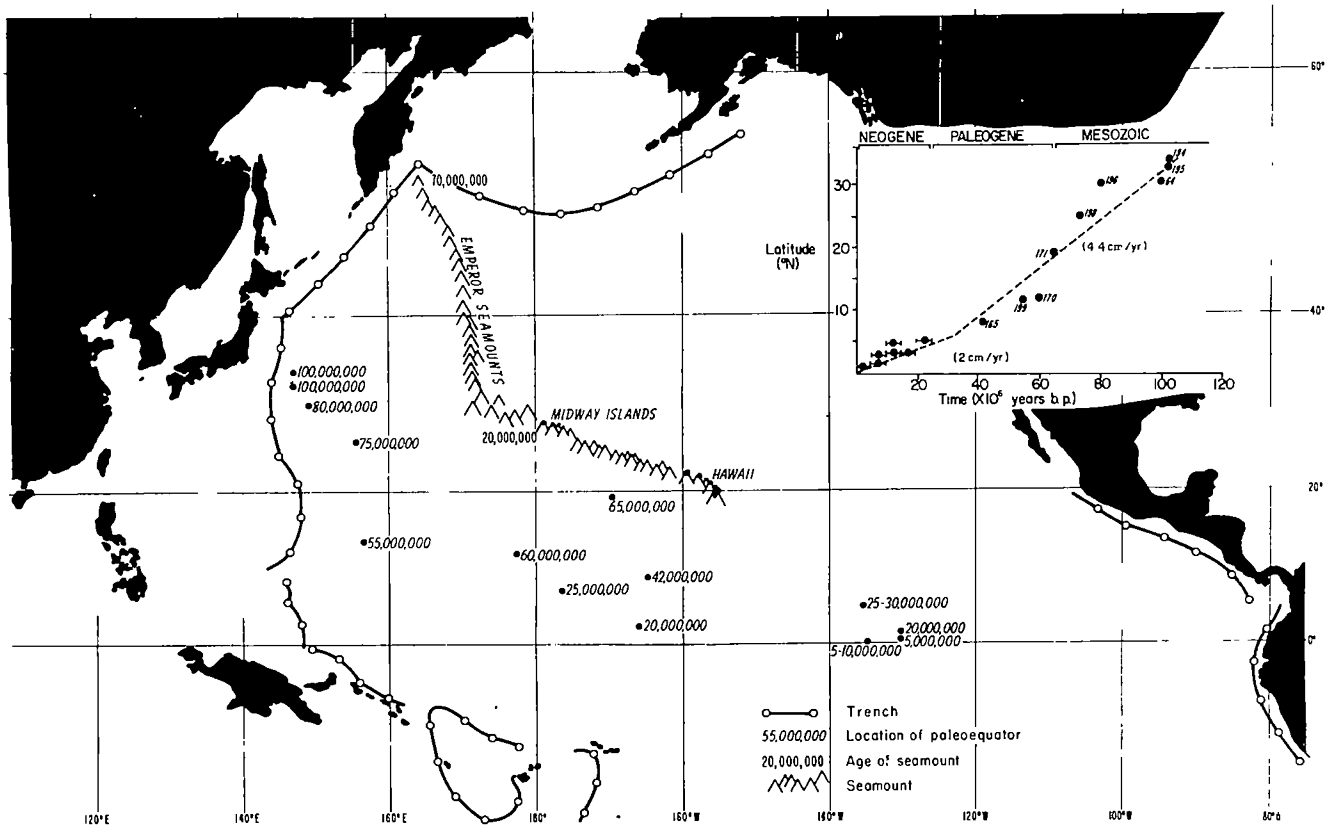

Fig. 3 Locations of palaeoequator in Pacific.

The age of the chert/chalk to abyssal clay boundary may thus be used as an index of the equatorial transit (Fig. 3). When combined with other evidence for equatorial transits[8-12] and the suggestion for a major change in the Pacific plate trajectory at about 30 m.y. (ref. 13), average northward components of plate motion of 2 cm yr^{-1} and 4.4 cm yr^{-1} are obtained for the Late Tertiary and the Early Tertiary to Cretaceous, respectively. Similar evidence of northward plate motion has been inferred from studies of the remnant magnetism of cored basalts and seamounts[9-12,14].

Thus, the mid-latitude and equatorial mid-ocean pelagic models, when combined, compare favourably with the drilling results of the northern Pacific. The Cretaceous chert/chalk sequence that lies beneath the Tertiary and Late Cretaceous abyssal clay in the northwestern Pacific records the earlier Mesozoic passage of the ancient Pacific crust beneath the equator. The Lower Cretaceous chert/chalk sequence that lies at the bottom of the northern holes apparently represents the initial basal chalk formed on new crust, and the abyssal clay that separates the 2 units records abyssal-basin sedimentation during the interval between the initial subsidence below chalk-line and the subsequent re-occurrence of chert/chalk deposition during the equatorial passage. The apparent success of the simple kinematic model in accounting for the stratigraphy of the western Pacific led us to examine more general implications of the model and to attempt a more analytical approach.

Analytical Model of Pacific Sedimentation

The following numerical values have been used in the calculation of the Pacific sedimentation models (Fig. 4): Crust formation at ridge crest at 3,000 m depth; compensation level at depth of 3,700 m; ridge crest subsides at rate of 35 m $(\text{m.y.})^{-1}$; sediment accumulation rates of biogenic sediments at 10 m $(\text{m.y.})^{-1}$; abyssal clay at 1 m $(\text{m.y.})^{-1}$, and equatorial biogenic sediments at an additional 10 m $(\text{m.y.})^{-1}$; zone of equatorial sedimentation 5° wide; trajectories of Pacific plate with a "westward" component approximately parallel to fracture zones, 259° and a northward component of 2 cm yr^{-1} from 0 to 30 m.y., and 4 cm yr^{-1} from 30 to 200 m.y.; and orientation of cross-sections at 79° intersecting 160° E at 0°, intersecting 160° E at 15° N, and intersecting 160° E at 30° N.

Basically the mathematics of the model is a simple bookkeeping operation. We consider as an example a section perpendicular to the ridge crest. Whatever the relative motion of the equatorial zone, it may be described by its speed and width projected on the section. At each step in time, the sediments accumulated at each location are calculated from the appropriate sedimentation rates, and added to the sediment thickness already there. Isochrons may then be drawn through the thickness generated to produce a model geologic section. Several parallel sections based on the same parameters give a complete history of sedimentation and vertical traces may then be compared with a bore hole from any locality (Fig. 4).

A model has been calculated for a profile across the Pacific from the modern ridge crest off California to the Mesozoic crust off the Mariana Arc (Fig. 3) and may be compared with the gross lithic stratigraphy reported from Pacific deep sea drilling.

Summary of Pacific Stratigraphy from DSDP Data

The basic data are shown as vertical columns from drill holes projected to the lines of section (Fig. 4). Fig. 5 illustrates an interpolated summary of the distribution of the different major lithologies in the Pacific.

A comparison of the model (Fig. 4) with the observed stratigraphy (Fig. 5) and stratigraphic summary (Fig. 6) shows good agreement. The Pacific crust ages from east to west; an observation justifying a basic assumption of the model. The basal chert/chalk unit is time transgressive increasing in age from east to west. In the eastern Pacific the basal carbonate is about 50 to 200 m thick (or about 20 to 40 m.y. in extent) indicating a general agreement with the model. The basal chert/chalk is interpreted as that accumulated at the ridge prior to its submergence beneath the compensation depth. An upper chert/chalk unit which is only present in the western Pacific is also time transgressive, increasing in age from the equator northwards, and from east to west, and is interpreted as the biogenic oozes accumulated during the passage of the Pacific crust beneath the equator. The upper and the lower chert/chalk units merge in mid Pacific with the existence of a chevron pattern as predicted by the model. Two abyssal clay units are observed. The lower unit consists of a wedge-shaped horizon, whose upper and lower boundaries are time transgressive. The base of the lower clay is the chert/chalk sequence accumulated at the ridge crest, and the top, the chert/chalk sequence deposited during the equatorial crossing. The upper clay unit is only found in the northern Pacific wedging out to the equator in the south, and the younger crust to the east.

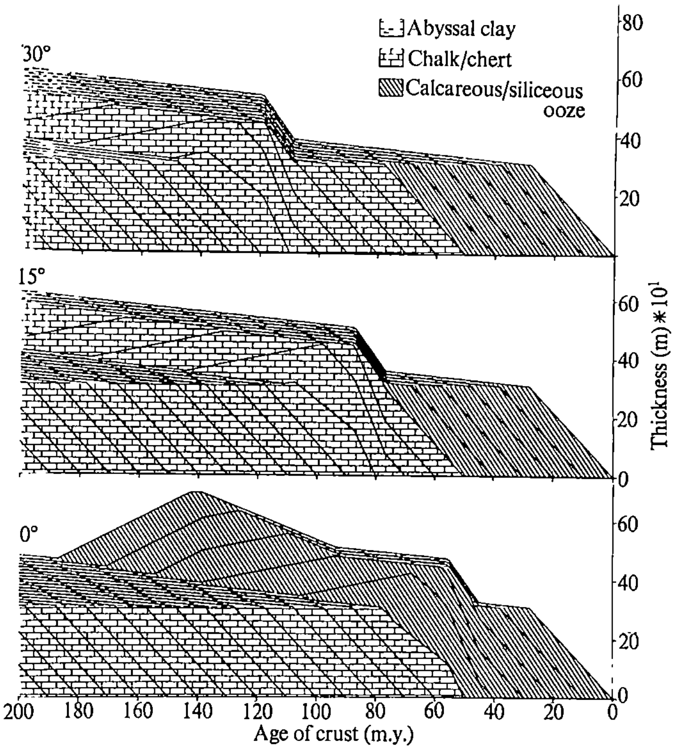

Fig. 4 Computed models of Pacific Ocean sedimentation history.

Other features observed in the data summary (Fig. 6) but not included in the model (Fig. 4) are that: Where the oceanic crust has passed marginal to a continental margin, positive area, or an extinct volcano we see the addition of turbiditic or volcanogenic sediments. Good examples are the wedge of turbidites along the west coast of North America[17–21], the turbidites filling the Caroline Abyssal Plain[4,5], and the wedge of wind blown volcanogenic debris east of the Asiatic arcs[4,5]. The presence of equatorial biogenic oozes along the whole length of the present equator, and the absence of this unit in any section south of the equator, and the onset of lithified chert/chalk sequences from calcareous and siliceous oozes at a crustal age of at least 50 m.y.

In general there is a close fit between the model and data summary both with respect to the distribution pattern, timing and thicknesses of the major lithologies. The fit is encouraging, and lends credence to the model as a useful first order approximation of the sedimentary history of the Pacific plate. Departures from the model should now illustrate smaller or more local events in the sedimentary history and add detail to the geologic history of the Pacific.

Acoustic Stratigraphy

The principal boundaries separating the lithologic units provide the strong contrasts in acoustic impedance necessary to create major reflectors of regional extent. Seismic reflexion profiling[22] has defined five acoustic units in the Pacific; an upper transparent layer lacking strong reflectors; a unit consisting of closely spaced strong reflectors known as the opaque layer; a lower transparent layer which is of smaller regional extent than the overlying layers; a lower opaque layer of limited extent; and basement, which, if smooth, is referred to as horizon B. The upper transparent layer corresponds to the abyssal clay in the west and central Pacific, turbidite sequences in the north and east, and unconsolidated biogenic oozes in drillings to the east and along the equator. The upper opaque layer corresponds to the thick chert/carbonate sequence of the western Pacific, the locally occurring lower transparent layer may correspond to the Cretaceous clay of deep sea drilling, and the lower opaque layer corresponds to the basal chert/carbonate in areas which having crossed the equator have acquired additional carbonates higher in the section.

Previous interpretations of the acoustic records evidenced a strong preference for the synchroneity of acoustic boundaries (that is, lithic boundaries), suggesting Eocene or Late Maestrichtian ocean-wide, or even world-wide, horizons apparently resulting from synchronous global events.

The top of the opaque layer is, however, widely time transgressive. Thus the former assumption of synchroneity simply does not conform to the evidence from deep sea drilling and is in conflict with the kinematic model of lithologic stratigraphy. Similarly, the assumption that the opaque layer is a clastic wedge has been disproved by the drilling results.

The acoustic data, stripped of the synchronous time-stratigraphic interpretation, can be compared favourably to the kinematic model. The upper opaque layer evidently is a chert/carbonate sequence deposited at least in part under equatorial conditions. The area of the Pacific in which the upper opaque horizon is observed is that portion of the crust which has passed under the equator (Fig. 7). The limits of the upper opaque layer are the equator on the south, the subducting trenches on the west, and a line, marking the limit of crust created subsequent to the equatorial passage, on the northeast. The opaque layer is apparently thickest between 20° and 30° N, a fact which may be explained by a smaller northward component of drift of the Pacific crust in Early Cretaceous time, an effect similar to that recorded for Neogene time by the equatorial sediment bulge.

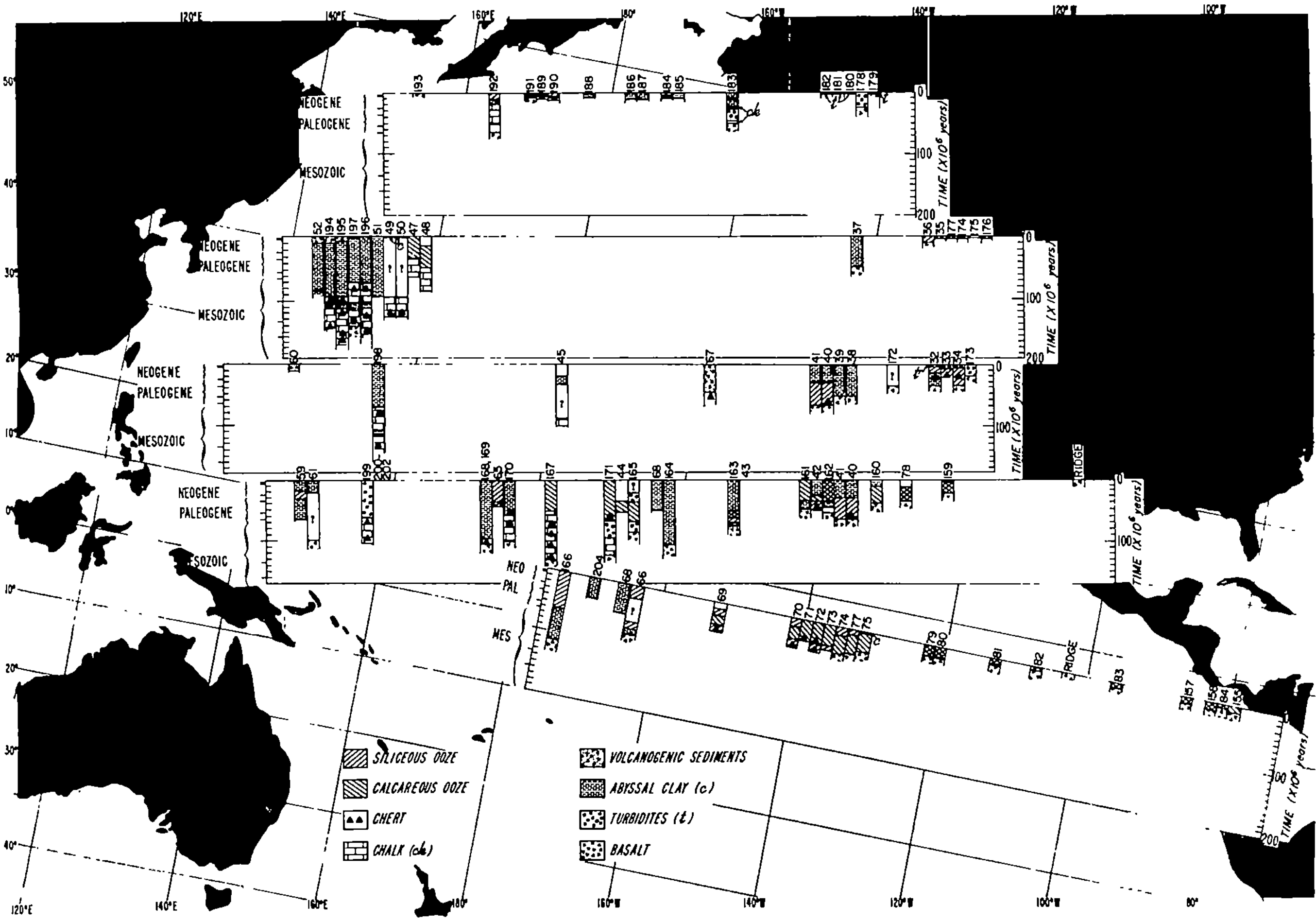

Fig. 5 Summary of drilling data from Deep Sea Drilling Project.

The upper acoustic opaque layer cannot be mapped in the northernmost western Pacific for the practical reason that the lower transparent layer pinches out a few hundred kilometres northwest of the Shatsky Plateau. This pinchout suggests that the basal carbonates merge with the equatorial carbonates and cherts, because the period of time separating the original generation of this crust and the equatorial transit of that crust was too brief to be represented by a layer of abyssal clay thick enough to be detectable by seismic reflexion profiling. Because the rate of abyssal clay deposition is so slow that a layer only 20 or 10 m thick is equivalent to 10 to 20 m.y., the true pinchout could be a considerable distance northwest of that shown by reflexion records. Thus somewhat northwest of the lower transparent layer pinchout would seem to have been formed very near the equator in pre-Hauterivian time.

The acoustic stratigraphy thus seems adequately accounted for by the kinematic model.

Certain further predictions can be made: First, on crust of a given age the total thickness of pelagic deposits should be markedly less in the South Pacific, which has yet to receive an equatorial contribution, than in the North Pacific where equatorial deposition has already produced an additional layer of carbonates; second, south of the equator cherts should be much less common than to the north.

Thus the new kinematic stratigraphy of pelagic deposits which predicts a characteristically diachronous behaviour of units can be applied to acoustic stratigraphy as well as to lithostratigraphy.

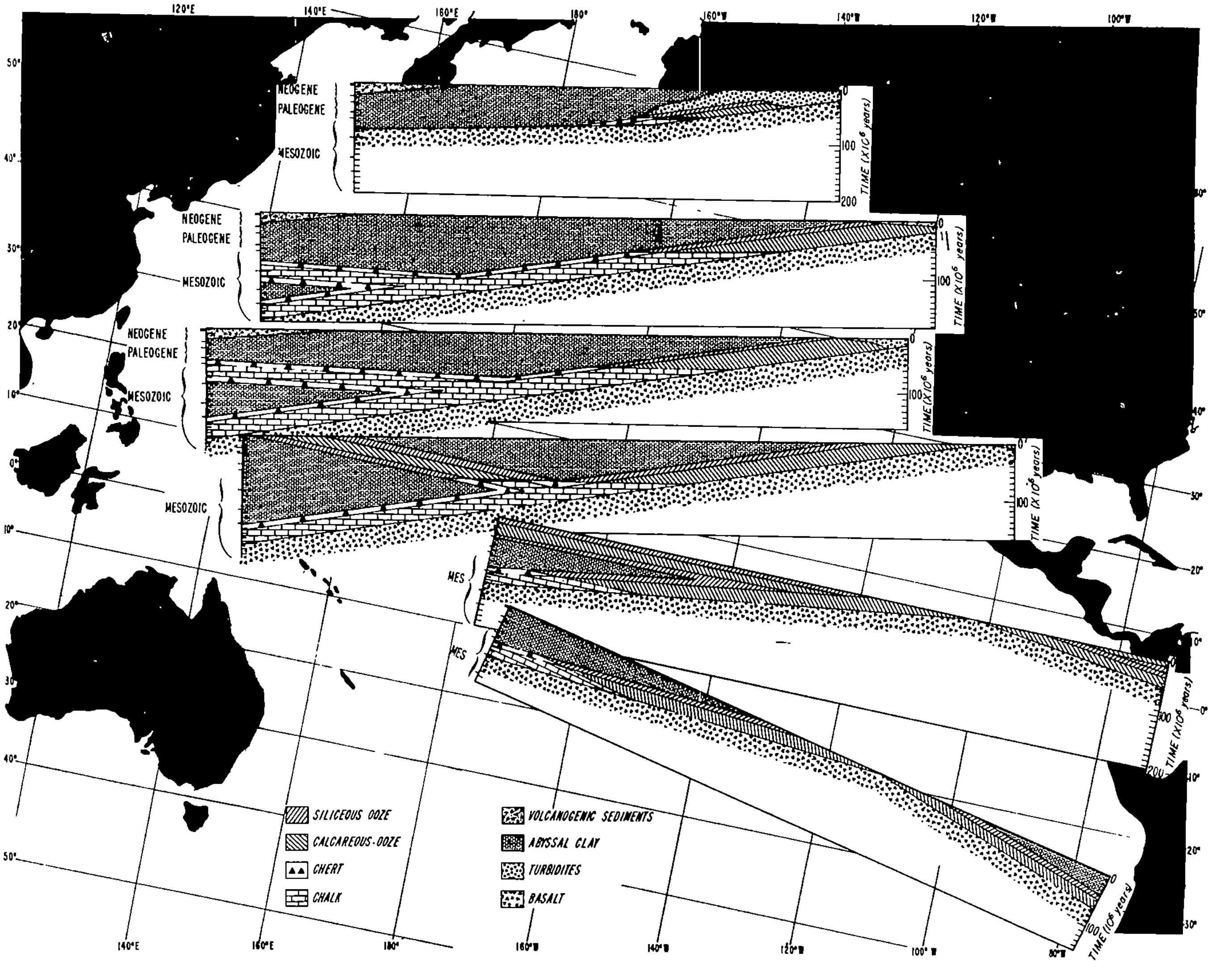

Fig. 6 Interpreted cross-sections showing sedimentary history of Pacific crust.

Magnetic Data

Stripe-like magnetic anomalies generated by east–west axial accretion are either absent or poorly developed in crust generated at the magnetic equator. A magnetically quiet zone has been mapped in the mid and high latitudes of the north central Pacific[23]. The zone which extends through the eastern Pacific from the present intersection of the magnetic equator with the axial rift valley towards the northwest Pacific (Fig. 7), lies somewhat east of the easternmost sites which sampled equatorial carbonates, and just east of the limit of the acoustic upper opaque layer. The magnetic quiet zone has been explained as a period in the Cretaceous during which magnetic reversals did not occur[23]. Although this explanation may be true in part, no data have yet been presented in the literature in clear support of this assumption. The kinematic model predicts that the magnetic quiet is the locus of crust formed under the equator. If there was indeed a period without reversals during the Cretaceous its effect would be to widen the apparent intersection and introduce other details.

The Pacific crust is divided into two regions, one formed before and a second after the equatorial crossing. The boundary between the two is the "magnetic quiet" zone (Fig. 7). Similarly, the restriction of thick opaque layers to the western Pacific results in the correlation of this region with that portion of the Pacific crust that has passed beneath the equator, and thus received a double layer of biogenic sediment.

Diachronous Detrital Deposits on the Margins of the Pacific Plate

Evidence of crustal motions may also be derived from diachronous volcanic deposits near plate margins. A detrital wedge of volcanic debris is found within 1,000 km of the

Asiatic arcs in the northwest Pacific (Fig. 6). The shape and extent of the wedge is a function of two counter balancing effects, the amount and extent of distribution of volcanic debris and the westward subduction of the Pacific plate. Assuming that the rates of both processes have been essentially constant during Late Tertiary time, equilibrium should result and the shape of the wedge would stay essentially constant. Near the distal edge of the wedge (sites 194, 195, 196), Late Tertiary sedimentation rates are approximately the same. Thus the difference in thickness of the wedge between sites may be ascribed purely to the older age of the initial deposition surface at the western sites. With the above assumptions a value of about 8 cm yr^{-1} is obtained for the westward component of drift of the crust, that is, the subduction rate into the marginal trenches. This rate is of the same magnitude as the axial accretion determined for the past few million years by the magnetic stripes at the crest of the Mid-Oceanic Ridge.

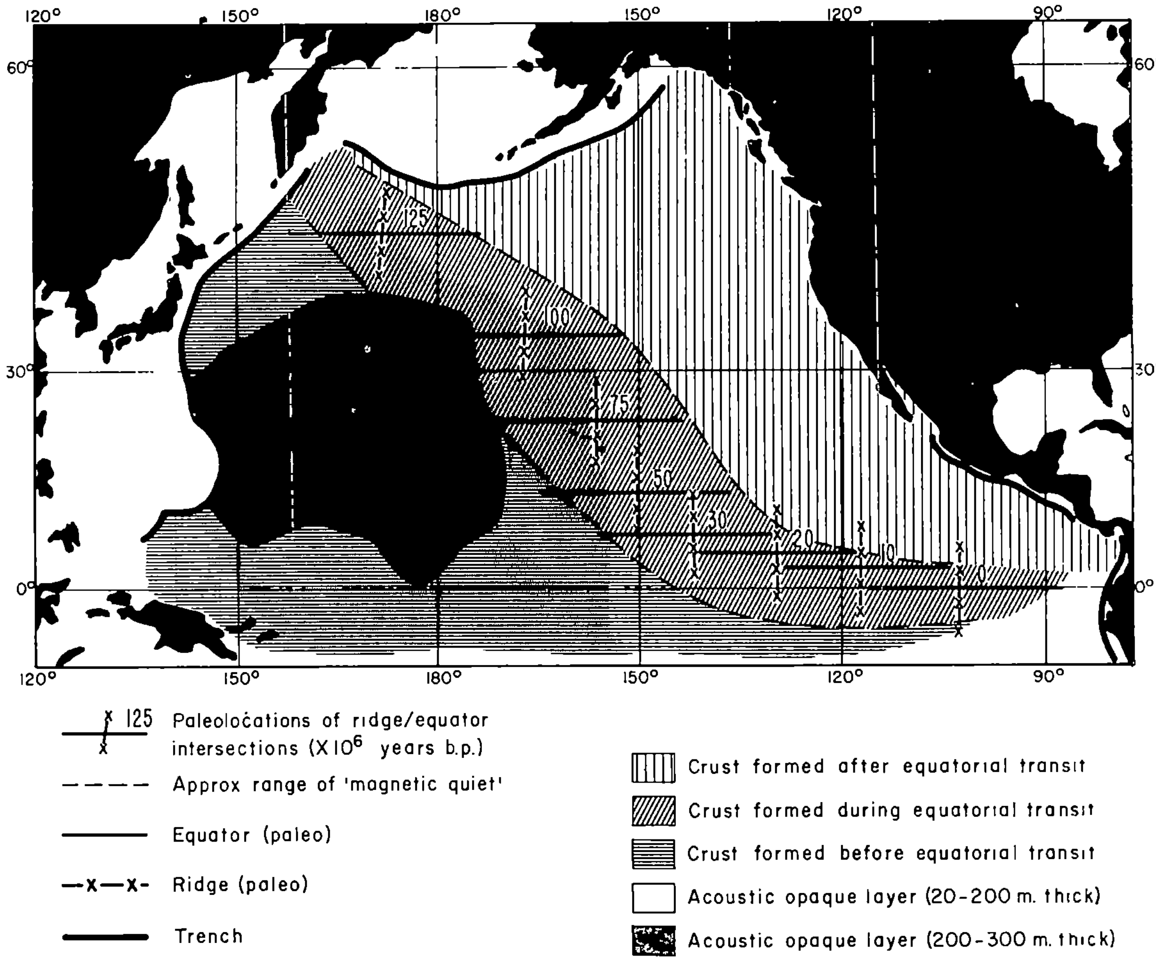
120°
150°
180°
150°
120°
90°
60°
30°
0°
125
100
75
50
30
20
10
0
125 Paleolocations of ridge/equator intersections (X10⁶ years b.p.)
Approx range of 'magnetic quiet'
Equator (paleo)
Ridge (paleo)
Trench
Crust formed after equatorial transit
Crust formed during equatorial transit
Crust formed before equatorial transit
Acoustic opaque layer (20-200 m. thick)
Acoustic opaque layer (200-300 m. thick)

Fig. 7 Age structure of the Pacific crust.

By contrast other marginal detrital deposits may be synchronous, that is, the cut off of turbidity currents to the relict Aleutian Abyssal Plain by the blockage of the Aleutian Trench[24], or the commencement of turbiditic deposition on the Caroline Abyssal Plain by the creation of a source area in the Caroline Islands.

Whereas detrital sediments deposited in the deep sea may by means of some catastrophic mechanism be broadly synchronous, the characteristic litho-stratigraphy of pelagic deposits is broadly and systematically diachronous. The history of the Pacific plate has apparently been governed by a few simple and systematic factors: the carbonate and silica compensation depth, the gradual sinking of oceanic crust and the northward migration of the Pacific crust beneath the palaeoequator.

While we are gratified by the apparent close agreement of data and model we wish to emphasize the severe limitations of both. The model presented here has ignored both the theoretical effect of reversals in plate motion on bed thickness and possible evidence of such reversals. We have considered only a few changes in direction and rate of crustal drift and ignored possible changes in sea level or compensation depth.

In our opinion a relatively small number of additional holes drilled in the more ancient parts of the ocean would provide data for a greatly refined model. It would seem that even with only a few dozen better located, well sampled bore holes in the ancient Pacific plate we could, with the aid of a kinematic model, arrive at a rather detailed history of the Pacific since the Jurassic.

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DNA Replication Sites within Nuclei of Mammalian Cells

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DNA replication can occur throughout the nucleus and is not restricted to the inner surface of the nuclear membrane.

THE involvement of a membrane site in DNA replication was first suggested by Jacob, Brenner and Cuzin[1] in their "replicon" model for replication of bacterial DNA, but the evidence accumulated since then is inconclusive. In prokaryotic cells, co-sedimentation of DNA replication points and cell membranes has been demonstrated[1–4], and the origin of replication and the membrane found to be associated[5]. A lipid-free replicating DNA-protein complex from *E. coli* has been isolated[6] and it has been reported that only the origin, but not the growing points, of the *E. coli* chromosome is attached to membrane[7].

In cell fractionation experiments with mammalian cells it was also found that replication points, detected by pulse-labelling with ^{3}H-thymidine (TdR), are associated with the nuclear membrane (or some other large, light, hydrophobic cell structure)[8–11,13]. Association between replication points and the nuclear membrane has also been detected by electron microscope autoradiography of thin sections through pulse-labelled, unsynchronized HeLa cells. The label associated with the membrane apparently moved into the nuclear interior after a 1 h chase[13].

On the other hand, most electron microscope autoradiographic experiments suggest that replication can take place throughout the nucleus. For instance, Comings and Kakefuda[14] generally found grains located throughout the nucleus when unsynchronized human amnion cells were pulse-labelled for 5 min or more with ^{3}H-TdR and then sectioned and autoradiographed. When, however, cells that were supposedly synchronized at the beginning of S phase were pulse-labelled for 5 or 10 min, grains were found predominantly over the nuclear membrane. Comings and Kakefuda concluded that initiation of replication takes place on the nuclear membrane, whereas the replication occurs anywhere within the nucleus.

Somewhat different results were obtained by Blondel[15], using KB cells and pulse times of 2 min; Williams and Ockey[16], using Chinese hamster cells and pulse times of 10 min or longer; and Erlandson and de Harven[17], using HeLa cells and pulse times of 15 min. All three groups concluded, in agreement with Comings and Kakefuda[14], that during a large part of the S phase grains are produced over the entire nucleus, but they differed from them in finding a peripheral pattern of grains more frequently at the end of the S phase than at the beginning. A cell fractionation experiment by Kay *et al.*[18] also demonstrated association of late-replicating but not early-replicating DNA with the nuclear membrane.

Higher Resolution Autoradiography

Regardless of the time in S phase at which replication occurs close to the nuclear membrane, one important implication of

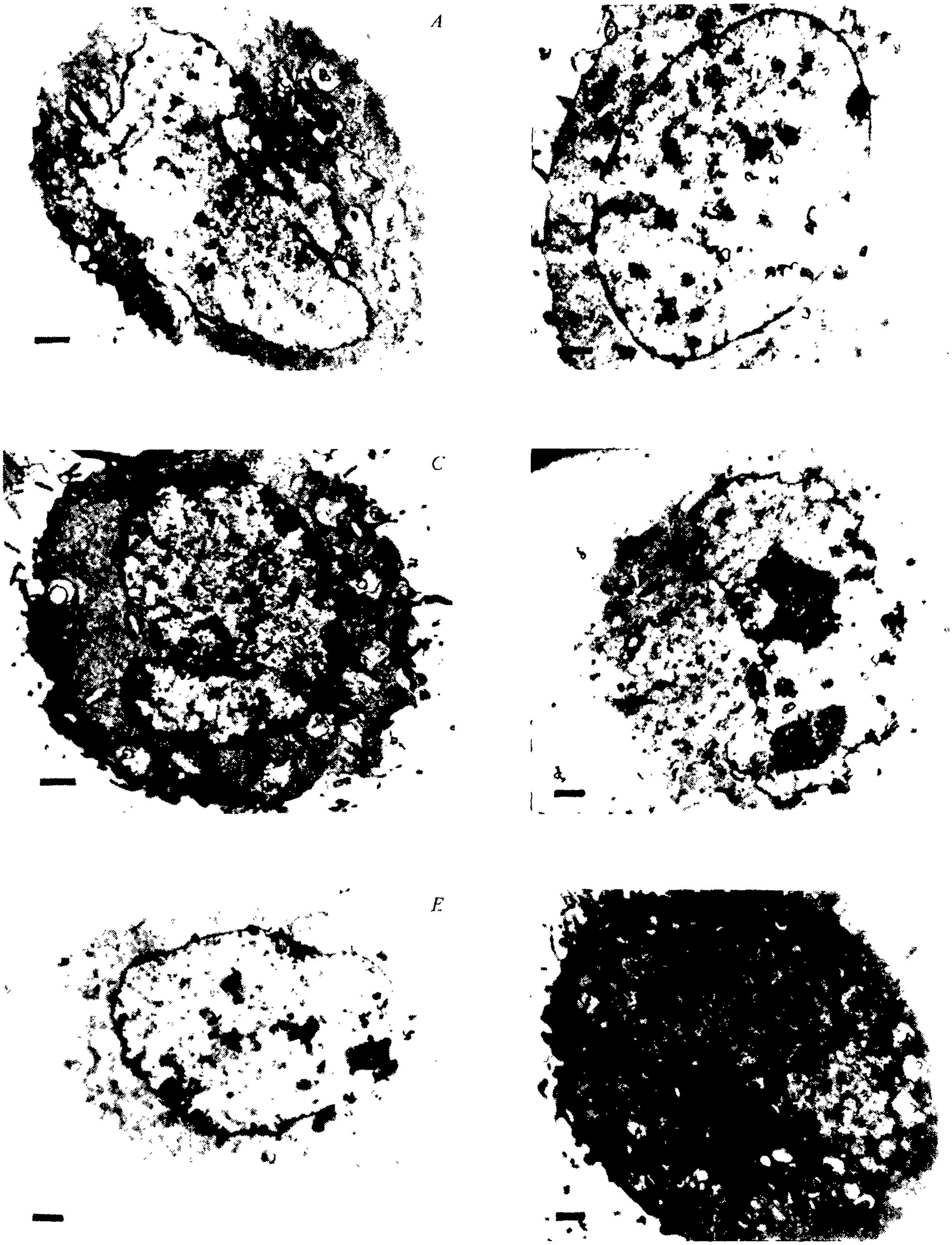

Fig. 1 Autoradiography of unsynchronized CHO cells exposed to ^{3}H-TdR for 0.5 min. *A* and *B*, grains distributed [illegible] nucleus. *C* and *D*, grains distributed around nuclear membrane. *E*, clustered grain distribution. *F*, mixed grain [illegible] CHO cells were grown on Petri plates in Joklik-modified MEM (Grand Island Biological Company) supplemented with [illegible] calf serum and non-essential amino-acids. Pulse-labelling was performed by first adding 5-fluorouridine deoxy[illegible] Hoffmann-LaRoche) to a final concentration of 1.6 μg ml.$^{-1}$ to inhibit further biosynthesis of dTTP. After 1 min [illegible] mmol^{-1}; New England Nuclear) was added to 17 μCi ml.$^{-1}$. After 30 s the plates were removed from 37° C, and the [illegible] sucked off. The plates were then washed with ice-cold isotonic saline containing FUDR at 0.1 μg ml.$^{-1}$ (two changes). [illegible] removed from the plates by trypsinization at room temperature in isotonic saline still containing FUDR. The cells were [illegible] then fixed with glutaraldehyde and OsO$_4$, dehydrated, embedded in epoxy resin[29] and cut into gold-purple sections [illegible] were mounted on grids and autoradiographed by the technique of Caro and Van Tubergen[20] except that the acet[illegible] was replaced with distilled water. Exposure time was 3.5 months. The bar in each figure represents 1 μm.

most of these electron microscope autoradiography experiments is that, in some parts of S phase, at least, replication occurs throughout the nucleus. How can this implication be reconciled with the experiments indicating that all replicating DNA is associated with the nuclear membrane? It is possible that a considerable amount of DNA is synthesized during a pulse as short as 2 min. Huberman and Riggs[19] have shown that the rate of DNA replication in Chinese hamster cells can be as much as 2.5 μm min^{-1}, although most replication seems to occur at rates between 0.5 and 1.2 μm min^{-1}. Thus as much as 5 μm of DNA could be synthesized during a 2 min pulse. If this DNA were synthesized at the nuclear membrane and then stretched out, it could reach the centre of a nucleus of diameter 5–8 μm and give rise to a false impression of the location of sites of DNA synthesis.

This effect could be ruled out by shorter pulses. We calculated that a pulse of 0.5 min would provide sufficient grains, after an exposure of several months, and the resolution (less than 1.25 μm of DNA synthesized) necessary to distinguish between replication solely at the nuclear membrane and replication elsewhere in the nucleus.

In most experiments, we used Chinese hamster (CHO) cells, which can be easily synchronized. The cells were pulse-labelled for 0.5 min with ^{3}H-TdR, then washed, fixed, embedded, sectioned and stained. The sections were placed on grids and autoradiographed by standard techniques[20]. After exposure times of several months, the emulsions were developed and the grids were examined by electron microscopy.

Sites of Replication

Cells from an unsynchronized culture, shown in Fig. 1, illustrate the variety of distribution of grains over the nucleus. The cells in Fig. 1*A* and *B* are labelled throughout the nucleus (general pattern), whereas the cells in Fig. 1*C* and *D* are labelled predominantly around the nuclear membrane (peripheral pattern). The grains in Fig. 1*E* are mostly clustered over regions of condensed chromatin, frequently near the membrane. Fig. 1*F* shows a cell with grains throughout the nucleus but with some concentration around the nuclear membrane.

Many grains are found in some cells more than 1.25 μm from the nuclear membrane (central grains), suggesting that replication is taking place at sites away from the membrane. To be certain of that conclusion, however, other possible explanations must be ruled out. The central grains cannot be due to background because few or no grains are found over the cytoplasm. They must be due to incorporation into DNA since no grains are found over G1 or G2 cells (see below), and the grains of isolated nuclei can be removed by DNAase. The central grains could also originate from DNA replication occurring on invaginations of the nuclear membrane either just above or just below the section plane. While this might explain some central grains, it certainly cannot explain most of them. Because the cells are sectioned with random orientations, we can get some idea of the frequency of invaginations which might bring nuclear membrane within 1.25 μm of the section plane from the frequency of invaginations in the nuclear periphery. Although some peripheral invaginations are evident in Fig. 1, they are not so frequent that most of the central area could be 1.25 μm or less from an invagination.

In some preliminary experiments we used HeLa cells, which have much more regular nuclei: central grains were also found over their nuclei (Fig. 2). Even serial sections up to 0.5 μm apart through a single cell all showed central grains. The change in pattern from general labelling in early S to peripheral labelling in late S suggests that general labelling is not an artefact of sectioning. Finally, the central grains cannot be accounted for by internal membranes within the nucleus. Such membranes have never been seen by other electron microscopists; apart from invaginations of the peripheral membrane we could see none in our sections.

To express quantitatively the proportion of cells showing peripheral labelling, we have modified the method of Williams and Ockey[16]. We defined central grains as those further than 1.25 μm from the nearest nuclear membrane, and peripheral grains to be those closer than 1.25 μm to the nuclear membrane. The "central activity" of a cell section was calculated as the ratio of the fraction of central grains : the fraction of nuclear area which was central. Nucleolar areas and grains were excluded because the nucleolus has less DNA than the rest of the nucleus. A histogram showing the frequency of various central activities for an unsynchronized cell population is shown in Fig. 3 (a central activity of 1.0 implies an equal concentration of grains over central and peripheral areas).

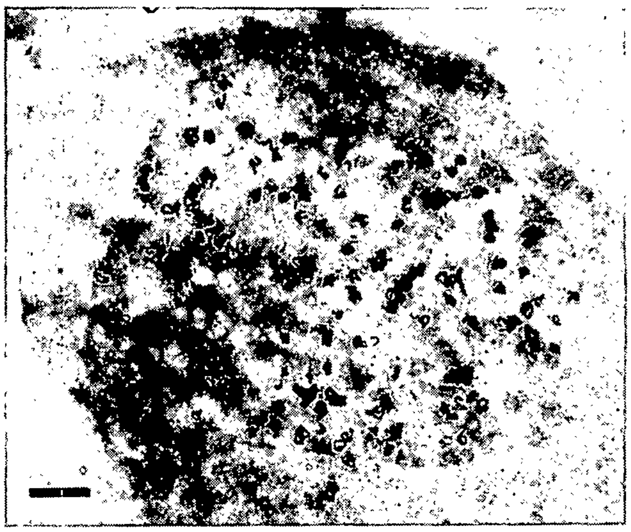

Fig. 2 Autoradiography of a HeLa cell exposed to ^{3}H-TdR for 1.5 min. The cells were grown in suspension culture in Joklik-modified MEM (Grand Island Biological Company) supplemented with 5% horse serum. Pulse-labelling was done by adding ^{3}H-TdR (20 Ci mmol^{-1}, New England Nuclear) to a concentration of 20 μCi ml.^{-1}. Exactly 1.5 min after addition of ^{3}H-TdR, the pulse was terminated by addition of an equal volume of ice-cold isotonic saline containing 1% glutaraldehyde. Subsequent processing was as in Fig. 1. Exposure time was 9.5 months. The bar represents 1 μm.

Only 13% of the cells in Fig. 3 have central activities of less than 0.25, showing that DNA synthesis can go on at sites away from the nuclear membrane. The nuclear membrane is therefore not essential for DNA replication in Chinese hamster cells. But the fact that many cells do show a predominantly peripheral pattern remains to be explained.

Peripheral Replication in Late S Phase

Since previous autoradiographic studies[14–17] had suggested that peripheral labelling occurs only at certain times during the S phase, we decided to try short pulse-labelling of cells synchronized to various times during the cell cycle. We chose 'Colcemid' reversal[21] to synchronize the cells. Growing cells were treated with 'Colcemid' for a few hours and the cells blocked in mitosis collected by selective trypsinization. These cells (90–100% mitotic) were allowed to continue growing in the absence of 'Colcemid'. Within 2 h, 98.5% of the cells completed division, and by 18 h after release from mitosis, more than 70% of the cells had divided again. We preferred this synchronization method to methods involving starvation of nucleotides[21], because cells recover excellently and normal DNA replication is not affected.

Table 1 and Fig. 4 show the distribution of grains within the nucleus as a function of time after release from mitosis. Peripheral labelling cannot be detected in the early stages of S but becomes predominant in later S.

Stable Location of DNA

If DNA is synthesized at the nuclear membrane (or other localized sites within the nucleus), then the DNA should move toward the membrane for replication and away from the membrane afterwards. The pattern of grains after a long pulse or pulse-chase should then be different from that after a simple short pulse. If, on the other hand, DNA replication can take place anywhere in the nucleus, then DNA movement is unnecessary and the grain pattern after pulse-chase labelling could be identical to that after simple pulse-labelling.

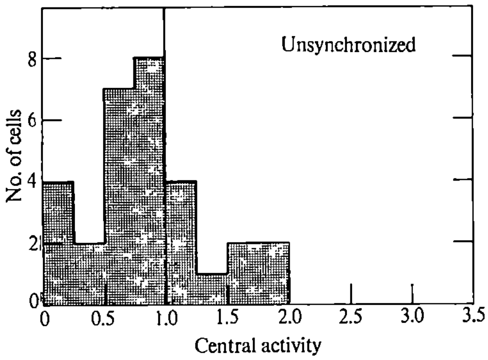

Fig. 3 Distribution of grains over unsynchronized CHO cells exposed to ^{3}H-TdR for 0.5 min. Prints at about ×15,000 magnification were made of autoradiograms of individual randomly chosen cells similar to and including those in Fig. 1. A line was drawn within each nucleus which was at all points 1.25 μm away from the nearest nuclear membrane. This line divided the nucleus into a central area and a peripheral area. Grains were counted over each area, and the size of each area was measured. In these determinations, grains lying over the nucleolus, and nucleolar areas, were ignored because the nucleolus has so much less DNA than the rest of the nucleus. Grains lying outside the nucleus were also ignored. "Central activity" was calculated as the ratio of the fraction of grains which were central to the fraction of area which was central. Thirty nuclei were measured for the histogram.

To test these possibilities, we first pulse-labelled synchronized cells for 0.5 min during the first half of the S phase (6 h after release from mitosis), and then chased with non-radioactive thymidine to late S phase (12 h after release from mitosis). Although the cells were examined in late S phase, they showed no higher proportion of peripheral labelling than expected for cells 6 h after release from mitosis (compare Figs. 4 and 5). In addition, unsynchronized cells pulse-labelled for 0.5 min show the same proportion of peripheral and general labelling as unsynchronized cells pulse-labelled for 10 min, or pulse-labelled for 0.5 min and then chased for 6.75 h (Fig. 5). In both of the chase experiments, the cells were more labelled after the chase than before, probably because incorporation of ^{3}H-TdR continues from the cells' internal pools.

Table 1 Extent of DNA Synthesis in Synchronized CHO Cells

Hours after release from mitosis	2	4	6	8	10	12	14
Percentage of cells labelled*	26	83	93	89	81	62	48
Average number grains/cell section after 1 month exposure†	<1	6	16	16	24	17	—

*Cells were synchronized as in Fig. 4. At 2 h intervals after release from mitosis, ^{3}H-TdR (20 Ci mmol^{-1}; New England Nuclear) was added to each plate (17 μCi ml.$^{-1}$ final concentration). After 10 min the cells were washed twice with cold isotonic saline, collected by trypsinization at room temperature, allowed to swell in hypotonic medium (2 mM $MgCl_2$, 1 mM EDTA, 10 mM KPO_4, *p*H 7.7) for 10 min, pelleted, fixed with methanol-acetic acid (3 : 1), spread onto subbed glass slides and allowed to dry. The slides were coated with autoradiographic stripping film ('Kodak AR-10') and exposed for 7 days. After development, the slides were stained with Giemsa stain, then mounted under 'Permount'. At least 312 cells were scanned to determine the percent of cells labelled at each time point.

†The total number of grains over each nuclear section was determined for the autoradiographs used in Fig. 4. These figures were divided by the exposure time in months. Extra data for 2 h and 8 h after release from mitosis are included here.

Thus DNA has a stable location in the nucleus. Because some of the unsynchronized cells must have divided during the chase, our results suggest that DNA bound closely to the membrane in one generation is also bound to the membrane in the succeeding generation.

Because we cannot detect any difference in labelling pattern between a 0.5 min pulse and a 10 min pulse, our results can be compared directly with those of previous investigators[15-17] who have used longer pulse times. Our results agree with most of the earlier results; a general-label pattern is obtained in early S phase and a peripheral one in late S phase[15-17], and chase experiments show that the nuclear position of DNA, once replicated, is stable[15,16].

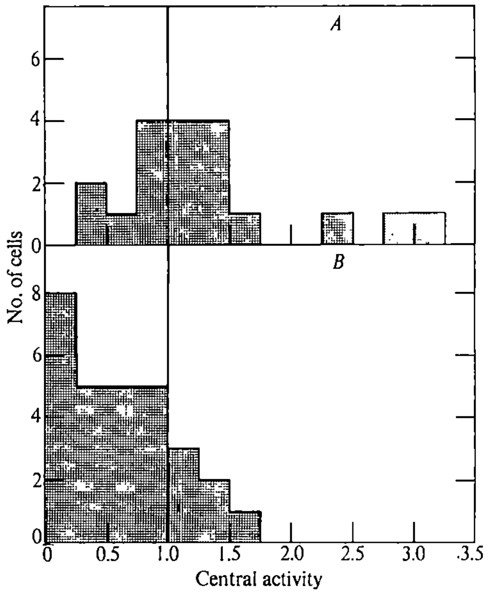

Fig. 4 Distributions of grains over synchronized CHO cells exposed to ^{3}H-TdR for 0.5 min. *A*, Early S phase (4–6 h after release from mitosis). *B*, Late S phase (10–12 h after release from mitosis). CHO cells were synchronized by the 'Colcemid' reversal method of Stubblefield. Pulse-labelling (performed at 2 h intervals after release from mitosis), preparation for electron microscopy, and autoradiography were performed as in Fig. 1. Exposure time was 2–4 months. Histograms were prepared as in Fig. 3. For *A*, eight nuclei pulse-labelled at 4 h and eleven nuclei labelled at 6 h after mitotic release were used. For *B*, thirteen nuclei labelled at 10 h and sixteen nuclei labelled at 12 h were used.

The increased labelling during chase experiments, together with an apparently lower rate of synthesis in early S phase (Table 1), suggests an explanation for the autoradiographic results of O'Brien *et al.*[13]. In their pulse experiment, generally-labelled cells in early S phase may have been overlooked because they have few grains per nucleus (and a more disperse distribution at that); the increased labelling provided by the chase would have made the generally labelled cells sufficiently obvious to count.

Initiation of Replication

Our results also partially disagree with those of Comings and Kakefuda[14]. They reported that cells synchronized to the beginning of S phase showed solely peripheral labelling. Williams and Ockey[16, 22] suggested that Comings and Kakefuda's results might be due to cell damage during the lengthy nucleotide starvation (24 h in the presence of excess thymidine and then 14 h in the presence of amethopterin) used to synchronize their cells. Indeed, the cytoplasms of the synchronized cells in Comings and Kakefuda's experiments contain many large vacuoles (indicating serious cell damage), whereas their unsynchronized cells have normal cytoplasm. Why cell damage should result in a peripheral labelling pattern is not clear. The unexpected pattern may be related to the finding[12] that polyoma virus infection causes mouse satellite DNA, which is normally late replicating[23-25], to replicate before bulk DNA.

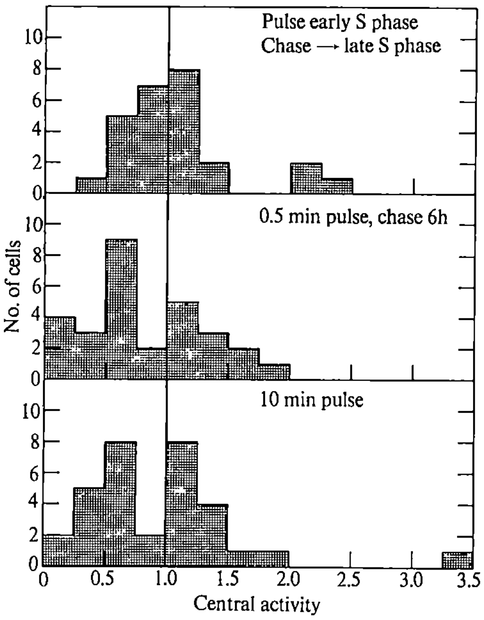

Fig. 5 Distribution of grains over CHO cells after pulse-chase or long pulse-labelling with ^{3}H-TdR. *A*, Synchronized cells (see Fig. 4) were pulse-labelled 6 h after release from mitosis as in Fig. 1. Then 30 s after addition of label, the medium was sucked off and the plates were washed, then replaced with medium containing 2.5 μg ml.$^{-1}$ of TdR. After 6 h the cells were collected by trypsinization and prepared for electron microscope autoradiography as in Fig. 1. Exposure time was 1.5–4 months. *B*, Unsynchronized cells were pulse-labelled as in Fig. 1 and chased for 6.75 h as in *A*. Exposure time was 3.25 month. *C*, Unsynchronized cells were pulse-labelled as in Fig. 1 except that the ^{3}H-TdR was left in contact with the cells for 10 min instead of 30 s. Exposure time was 1.5–6 months. In all cases, histograms were prepared as in Fig. 3. For *A*, twenty-four cells were used, whereas for *B*, twenty-nine cells were used, and for *C*, thirty-two cells were used.

Because Comings and Kakefuda's[14] results must be discounted owing to cell damage, it seems that DNA synthesis can occur throughout the nucleus, and the nuclear membrane is not involved in initiation of replication. We have found, however, that in very early S phase (2 and 4 h after release from mitosis), the rate of replication per cell (measured as the average number of grains per nuclear section over labelled nuclei after a fixed exposure time) is much less than in later S phase (Table 1). This suggests that at the true beginning of S phase, the rate might be so low that we cannot detect labelling, let alone determine whether the pattern is peripheral or general.

Euchromatin and Heterochromatin

Heterochromatin has been shown to be replicated later than euchromatin and is condensed during interphase[26,27]. Our sections and those of others[14-17], show a preponderance of condensed chromatin attached to the inner nuclear membrane. Thus our results are consistent with the notion[16] that euchromatin is replicated early in S phase and is distributed throughout the nucleus, whereas heterochromatin is replicated in late S phase and is condensed along the inner nuclear membrane and in other discrete areas.

Reinterpretation of Cell Fractionation Experiments

Whereas many of the cell fractionation experiments on the intranuclear location of DNA synthesis[8-11,13] have been interpreted in favour of attachment of replication sites to the nuclear membrane, this is not the only possible interpretation. Equally valid is the possibility that, after cell lysis, special structural properties of the growing points (extensive single strandedness, for instance) might result in their binding more protein, membrane, or other material than bulk DNA. Alternatively, the growing points may actually be attached inside the cell to some material that causes their separation from bulk DNA during lysate fractionation.

As experiments with mammalian[8-11,13] and bacterial[2,3,5] cells used similar techniques and gave the same results, it is possible that the growing point in bacteria may also not be attached to the membrane.

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Note added in proof. Fakan *et al.*[28] have recently obtained results similar to ours in both autoradiographic and cell fractionation experiments with mouse cells.

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LETTERS TO NATURE

PHYSICAL SCIENCES

2.8 cm Radio Emission from α Orionis, HBV 475 and MWC 349

We have used the Max-Planck-Institut 100-m telescope to search for radio emission from stars that are believed to have ejected or to be ejecting matter. Eight known radio stars were on our observing list and all were detected. Three others, α Ori, HBV 475 and MWC 349, were also detected. Three others were possibly detected, but need further observations for confirmation. For 17 others we obtained no signal significantly greater than the r.m.s. noise. This communication concerns the three definite new detections.

The telescope was equipped with a cooled parametric amplifier at 10.68 GHz with an overall system noise temperature of about 120 K. The half-power-beam-width of the telescope is about 80 arc s and the aperture efficiency is about 40%. The pointing of the telescope is repeatable to a few arc s.

We used two observing methods. First, we made so-called on-off measurements in the beam switching mode. This results in doubling the signal of the source compared to conventional single-beam observations. The two beams were separated by 3 min 11 s and positioned symmetrically about the focus. The beams were pointed alternately to the star position. The total integration time for one "on" or one "off" was 2 min. At least four "on-offs" were made for each source. Second, if there seemed to be a positive signal in the beam-switching measurements, we scanned in two perpendicular directions through the position of the star. The length of a single scan was 10 arc min. After several scans the two horns were turned through 180 arc deg. In this way, the sign of the observed signal at the two beam positions in the scan was reversed. We consider the results obtained with the scan-method to be more significant than those obtained by the beam-switching technique; it is possible for random signals to simulate a positive detection in the beam switching, but it is highly unlikely that random signals will simulate the double beam response pattern in the scanning mode.

The data were obtained during the nights of October 28 and 31, 1972. The weather was stable and the nights clear. The r.m.s. noise after two minutes of integration corresponds to 4 mf.u. and is apparently due to system noise and not to confusion.

Table 1

Source	date	Method	$S_{10\cdot68}$ (mf.u.)
α Ori *	72–10–29	On-off	9±4
α Ori †	72–01–01	Scan	7±1
HBV 475 *	72–10–28	On-off	12±4
HBV 475 ‡	72–10–31	Scan	8±1.5
MWC 349¶	72–10–28	Scan	460±50
MWC 349¶	72–10–29	Scan	300±40

* The error quoted is the r.m.s. deviation for a single on-off; twelve such measurements were made.

† The average of 240 scans; the error quoted is the r.m.s. deviation from the fitted double beam pattern (see Fig. 1*a*).

‡ The average of 120 scans; the error quoted is the r.m.s. deviation from the fitted double beam pattern (see Fig. 1*b*).

¶ The error quoted reflects the uncertainty in the calibration rather than being due to noise.

α Orionis: Weyman and Chapman[1] predicted detectable radio radiation from α Ori. Two searches were made in 1966 (refs. 2, 3) at frequencies close to ours. They gave some evidence of positive results on some occasions. Kellermann and Pauliny-Toth[2] obtained a positive result on one night, but eleven subsequent trials gave no detectable signal. The positive result obtained by Seaquist[3] was apparently obtained during only one night. The signal to noise ratios of the detections never exceeded four. Further, the observations were all made with the on-off method only, with the inherent possibility of spurious signals. Thus, it remained uncertain whether the detections were real, or whether α Ori is a variable radio star.

The average of our azimuth scans through α Ori is shown in Fig. 1*a*. The flux derived is well below the values quoted by previous observers[2,3]. We suggest that it represents the normal radio intensity of α Ori at this frequency, and that previous observers have detected outbursts in which the flux was temporarily higher. This suggestion is supported by the fact that we found no significant difference between the two observations made three days apart, whereas all other detections of radio stars have indicated that their fluxes are variable with time scales shorter than three days.

Our value for the flux from α Ori is less than that predicted by the model of Weyman and Chapman by a factor of 10. Hjellming and Wade[4] obtained a negative result at 3.7 cm. If the flux at that wavelength is also a factor of 10 less than predicted, it would be just below their detection limit. Thus, it is possible that Weyman and Chapman's model correctly predicts the radio spectrum but is in error by a scale factor affecting the intensity.

If we assume a diameter for the source of 0.034 arc s, as quoted by Brown[5] for the diameter of the star, it follows that the brightness temperature of the source must be about 10^5 K. If we assume, on the other hand, that the brightness tempera-

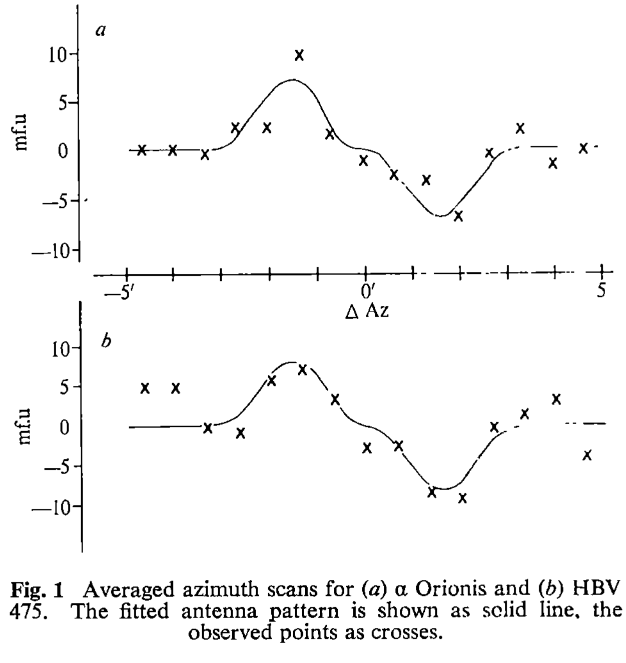

Fig. 1 Averaged azimuth scans for (*a*) α Orionis and (*b*) HBV 475. The fitted antenna pattern is shown as solid line, the observed points as crosses.

ture of the source is that of the photospheric temperature of the star, namely 3,500 K, we obtain a diameter of 0.18 arc s for the source, a value which is only about five times the diameter of the star. The real values of the size and brightness temperature of the source will certainly lie between these limits.

HBV 475: The variability of this star was discovered by Kohoutek[6]. Its spectrum is peculiar and contains emission lines[7]. Its light curve shows a slow but steady increase in brightness over the past 30 yr with the rate of increase being greater during the past five years. It seems likely that the increase in brightness is associated with an increase in the size of the star.

We detected radio emission on both of the two nights that observations were made (see Table 1). The average of our scans in azimuth is shown in Fig. 1*b*. We tentatively suggest that the radio emission originates in an extended atmosphere which also emits the optical emission lines.

MWC 349: A radio source within 1 arc s of the position of this peculiar Be star was reported by Braes, Habing and Schoenmaker[8,9]. At 1,415 MHz they obtained a flux density value of 60 mf.u. We have the impression that the change in flux density from the night of October 28 to the night of October 29 is real, and that MWC 349 is a variable radio source, possibly of the Antares type.

We acknowledge the support of the technical divisions of the Max-Planck-Institut für Radioastronomie, and thank Dr I. Pauliny-Toth for supplying his stacking program and Dr L. F. Smith for reading the manuscript.

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5 GHz Observations of the Infrared Star MWC 349, and the H II Condensation W3(OH)

Braes, Habing and Schoenmaker[1] have detected radio emission from MWC 349, the flux density at 1,415 MHz being 0.060 ± 0.007 f.u. They also summarize the remarkable properties of this star, which is believed to be an early B-type star[2] with some 10 mag of obscuration and with a strong IR excess, which may be associated with a surrounding dense cloud of gas and dust[3,4].

We have observed the source with the 5-km radio telescope at Cambridge, and find it to have a flux density at 5 GHz of 0.22 ± 0.01 f.u. The source is slightly extended (Fig. 1), and by fitting a model to the two-dimensional visibility function may be approximated by a uniform circular brightness distribution with an angular diameter of 2.4 ± 0.2 arc s, although there is a weak extension in position angle 240°.

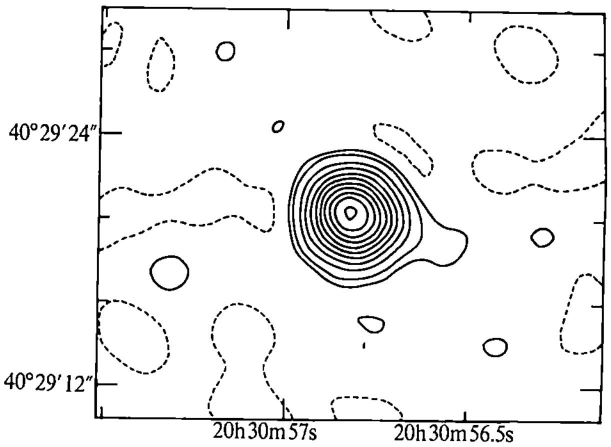

Fig. 1 Contour map of MWC 349 at 5 GHz. The contour interval is 0.0075 f.u. but the contours at $+\frac{1}{2}$ and $-\frac{1}{2}$ (dotted) of this interval are also shown.

The position of the centre is:

$$\left.\begin{array}{r}20\text{ h }30\text{ min }56.84\text{ s}\pm0.01\text{ s}\\ 40^\circ\ 29'\ 20''.38\pm0''.10\end{array}\right\}1950.0$$

The optical position of MWC 349 measured at Leiden is 0.9 arc s N of this position but new observations recently made by Yallop (Royal Greenwich Observatory) give a provisional position

$$\left.\begin{array}{r}20\text{ h }30\text{ min }56.855\text{ s}\pm0.01\text{ s}\\ 40^\circ\ 29'\ 20''.40\pm0''.1\end{array}\right\}1950.0$$

The agreement with this new position is very satisfactory. The angular size and flux densities of the source at 1.4 and 5 GHz are consistent with thermal emission from a region having an electron temperature (T_e) of 9,000 K and an emission measure of 2.7×10^7 cm^{-6} pc. The errors in the low frequency flux density and the angular size correspond to an uncertainty in T_e of ±2,000 K. The close similarity of this temperature to the value of 10,000 K found for many H II regions gives strong support for a thermal explanation for the radio emission from MWC 349.

Taking a distance of 2.1 kpc as suggested by Reddish[5] on the basis of the possible association of MWC 349 with the Cygnus OB 2 association, the diameter of the radio source is 0.024 pc and the electron density 3.4×10^4 cm^{-3}, corresponding to a mass of ionized gas of 9×10^{-3} $M_\odot$.

Because the source is optically thin at 5 GHz, we use the formula given by Rubin[6] to obtain the total number of Lyman continuum photons emitted from such a region at a temperature of 9,000 K. This gives $L_c\sim9\times10^{46}$ s^{-1}, suggesting that MWC 349 is of spectral type BO or earlier.

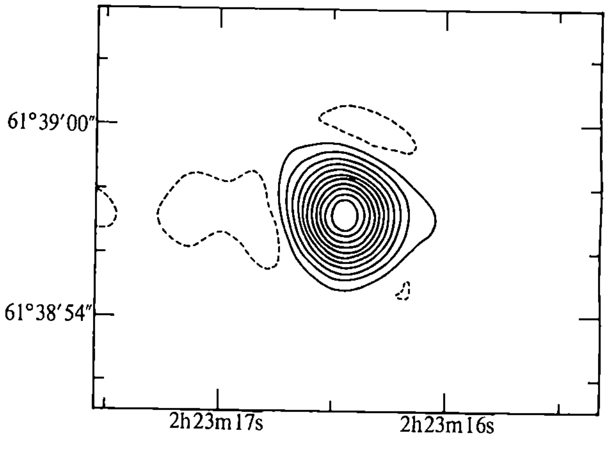

Fig. 2 Contour map of W3(OH) at 5 GHz. The contour interval is 0.040 f.u.

It is of interest to compare this source with the continuum emission from W3(OH), the compact component associated with OH emission in the H II region W3. This component has also recently been observed with the 5-km telescope (Fig. 2). The position of the centre is:

$$\left.\begin{array}{r} 02\text{ h } 23\text{ min } 16.44\text{ s} \pm 0.01\text{ s} \\ 61^\circ\, 38'\, 57''.18 \pm 0''.10 \end{array}\right\} 1950.0$$

The total flux density at 5 GHz is 0.62±0.02 f.u. and nearly all of the emission originates in a compact elliptical component whose diameters are (1.9±0.2 arc s) and (2.3±0.2 arc s) with the major axis in position angle of about 60°.

Earlier observations of W3(OH) by Wynn-Williams[7] with the 1-mile telescope showed that the source had dimensions of <4.5 arc s $\times <5.2$ arc s. He derived a model which fitted these observations and accounted for the spectrum. Assuming a distance of 3 kpc and an electron temperature of 10^4 K he concluded that the source was of diameter 0.024 pc and contained a total mass of ionized hydrogen of 0.042 $M_\odot$.

In the light of the new data these figures must be slightly revised; the compact component has dimensions of 0.027×0.033 pc. Because the compact component is optically thick at 5 GHz (ref. 7) the observations may be used to derive an electron temperature of 10,000±1,000 K. Using the spectrum of Wynn-Williams *et al.*[8] we obtain a central emission measure of $\sim 4.7 \times 10^8$ pc cm^{-6}, and a mass of ionized gas of 0.068 $M_\odot$. Using the 86 GHz point shown on the spectrum in ref. 8 we obtain $L_c \sim 2.5 \times 10^{48}$ s^{-1}, indicating that there is probably a central exciting star of type 07 or earlier.

Cooper, Davies and Booth[9] have measured the relative positions of 16 components of the 1,665 MHz emission from W3(OH). Although the positions are not absolute the mean position determined by Raimond and Eliasson[10] for the 1,665 MHz emission lies within a few arc s of the centre of the continuum source. We suggest that the OH components determined by Cooper *et al.* may be located around the periphery of the continuum source as shown in Fig. 3. This distribution strongly supports the model of stimulated OH emission proposed by Cook[11,12] who concluded that the emission will occur only where there is a long path-length in the line of sight in a medium of low temperature and small velocity dispersion; at the same time the region must lie close to the boundary of the H II region. The observed absence of OH sources within the disk of the H II region, and their confinement within a narrow strip round the edge agrees well with this model.

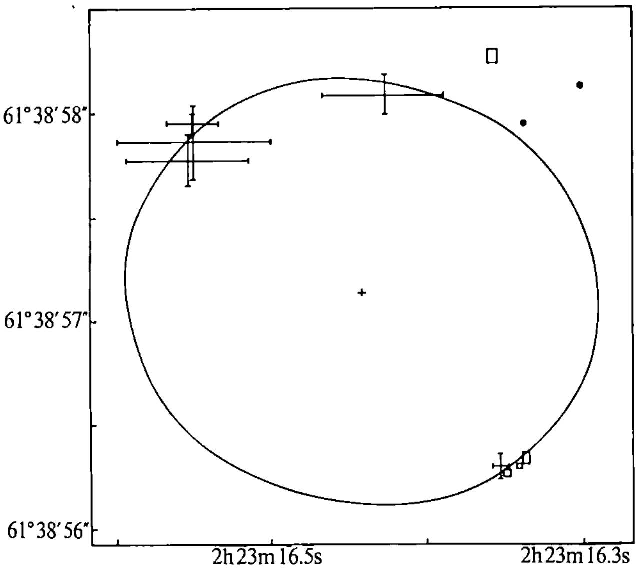

Fig. 3 Map showing the elliptic model of the W3(OH) continuum source fitted to the relative positions of the OH components[9]. The errors in the relative positions of the OH sources are indicated by error bars; the errors in the radii of the ellipse are ±0.1 arc s in any position angle.

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Solar Electrical Discharges

HEMENWAY *et al.*[1] state, "We conclude that most of these submicron particles have come from the Sun, although this hypothesis poses formidable problems". These problems do not arise if the white streaks which can clearly be seen in the perimeter of sunspots are electrical discharges, because the temperature at points between or remote from these discharges at their level is low enough for particles to form and radiation pressure would cause some of them to be ejected. The presence of atmospheric particles generally leads to the formation of electrical charges[2].

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Response of a General Circulation Model of the Atmosphere to Removal of the Arctic Ice-cap

OVER the past few years, numerical models have been developed for investigating the general circulation of the atmosphere and studying its long term behaviour. (See, for example, Smargorinsky *et al.*[1], Kasahara and Washington[2].) These models are firmly based on the equations of fluid motion and thermodynamics and simulate in mathematical terms the chief physical processes which are thought to be of importance in determining large scale atmospheric motions over long periods of time (a month or more). The advent of very high speed computers has made numerical experiments with these models reasonably easy.

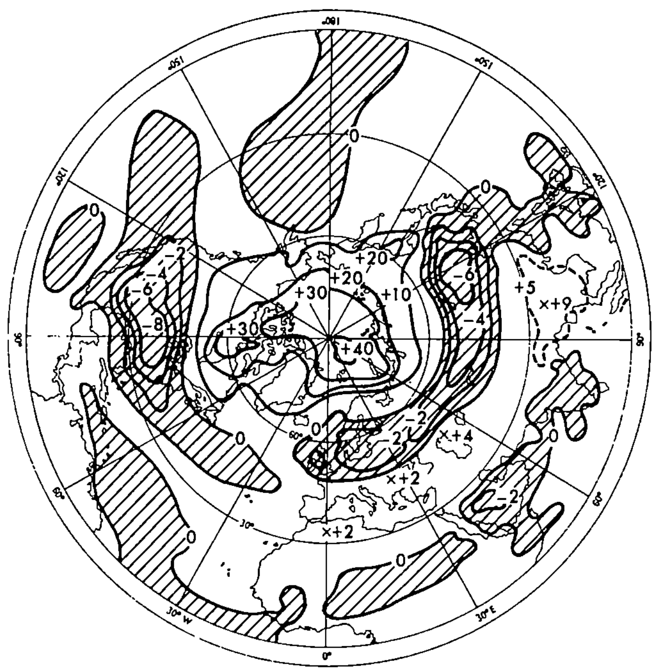

Fig. 1 Temperature differences, in °C near the model surface, between the computation with an ice-free arctic and the computation with ice at the mean climatological position. Hatched areas indicate regions of cooling in the ice-free experiment.

One model has been described in detail by Corby *et al.*[3]. The mode of computation essentially consists of integration forward in time from an initial state for a considerable number of model days using physical parameters appropriate to a given season and obtaining the mean seasonal state by averaging the later computed states; in the experiments described here the model was integrated forward in time for 80 days under winter conditions and the mean seasonal state obtained as the average of the last 40 days.

It is possible to vary the model to determine its reaction to substantial changes in the assumed physical properties. In one of these variants the region of winter arctic ice, as defined by the mean climatological position, was replaced by open ocean maintained at freezing temperature; what had been a surface with a temperature determined by radiational balance became a surface of constant temperature. The results of computations with ice and with open ocean differ quite considerably. The most marked difference is, of course, the great warming of the lower layers of the troposphere over the arctic basin, where, in the ice-free arctic experiment, there was an oceanic reserve of heat to balance radiative losses; this was to be expected. It might also have been expected that in mid-latitudes temperatures in the lower atmosphere would be raised. In fact, there is a lowering of mid-latitude continental temperatures near to the surface but with little change over the sea where the mean sea surface temperature had been left unchanged. This result is illustrated in Fig. 1, which shows the temperature difference between the two computed seasonal means at the level in the model most representative of the surface. The changes are considerable. The mid-latitude cooling may be compared with the temperature anomaly of −5° C in the very severe January of 1963; a temperature anomaly of −2° C would indicate a very cold winter month.

Other results from these experiments show a distinct southward displacement and weakening of the prevailing mid-latitude westerlies when there was no polar ice-cap, and this is similar to the result obtained from another ice-free arctic general circulation experiment conducted with the Mintz-Arakawa model[4]. What seems to happen is that the general decrease of temperature gradient between equator and pole reduces the strength of westerly flow in mid-latitudes and, there, the circulations become more blocked. Consequently regions which at present benefit climatically from the westerlies might be cooler in an ice-free arctic regime.

I do not claim that these results necessarily indicate what might happen in the real atmosphere, because the model itself has several shortcomings, and one should not dwell on the results in particular areas because they are almost certainly not quantitatively correct. The sign of temperature changes in mid-latitudes is perhaps rather unexpected, and the results illustrate that qualitative arguments may be deceptive and unreliable in considering a physical system as complicated as the atmospheric circulation which includes so many non-linear interactions and feed-back mechanisms.

Considerable refinement and elaboration of numerical models will be required before their answers to questions of the kind raised in this letter can be accepted with any confidence. Nevertheless the potential superiority of the numerical approach for the investigation of problems of climatic modification is beyond doubt.

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Deep-sea Sediment Source Areas: Implications of Variable Rates of Movement between California and the Pacific Plate

Recent work has indicated acceleration of motion on the San Andreas Fault[1], but previous studies have not delineated variable rates of motion with time between the Pacific and American plates. Offsets on the San Andreas and associated fault systems yield a mean rate of motion for a given period of time and deal with motion within the area of a wide plate boundary; therefore, these do not show total relative motion or variations in velocity between the two plates[2]. Magnetic anomalies can be used to measure the total relative motion and variations in velocity between the two plates. But magnetic anomalies at the mouth of the Gulf of California represent only the past few million years of movement which has been going on for at least 25 m.y. (ref. 3). Here I describe a method by which the amount and rates of motion between California and the Pacific plate with time can be determined.

The Delgada submarine fan lies off northern California, south of the Mendocino Fracture Zone, and is at least Oligocene in age[4]. The fan lies in a unique position on the eastern edge of the Pacific plate directly adjacent to the varied lithology of source areas on the American plate to the east. If the fan has passed source areas of distinctive lithologies on the American plate, then its stratigraphy may indicate the amount and rate of movement between the two plates. This area is particularly well located for such a study because there is no land mass (source area) between the fan and the margin of the Pacific plate and because the Mendocino Fracture Zone inhibits the introduction of sediment into the fan area from the north[4]. Therefore changes in sediment composition may indicate the position of the fan relative to these distinctive source area rocks on the American plate.

Semi-quantitative X-ray diffraction studies of the less than 2 µm fraction[5] from sites 32, 33 and 34, Leg V, of the DSDP, reveal significant changes in the percentages of the various clay minerals with time. The changes in percentages of kaolinite+chlorite/illite/montmorillonite occur at approximately 4 m.y., 5 m.y., 9 m.y. and 15 m.y. (Table 1).

Changes in the detrital coarse fraction mineralogy, amphibole and pyroxene assemblages and changes in degrees of stress and strain indicated by stretching and undulatory extinction show significant changes during these same time periods (manuscript in preparation).

Table 1 Computer Analysis of Maximum Variations in Percentages of Clay Minerals from Leg V, Sites 32, 33 and 34, DSDP

Absolute age (m.y.)	Chlorite and/or kaolinite	Illite	Montmorillonite
0			
2	48%	42%	7.5%
4			
6		30%	26%
8	32%	52%	16%
10			
12	Clay minerals occur as a trace component of the less than 2 µm fraction		
14			
16	14%	42%	46%

The Delgada fan is assumed to be one basin of deposition and to have been built by turbidity current and hemipelagic deposition from continental source areas. A simple model of evolution of the fan can be constructed so that the changes in mineralogy and style of deformation of mineral grains are consistent with the changing source areas (Fig. 1). Important source areas in this model, schematically represented in Fig. 1, include: Northern Coast Ranges from Holocene to 4 m.y.; north-central Sierra Nevada from 4 m.y. to 5 m.y.; eastern Santa Cruz Mountains–northern Diablo Range from 5 m.y. to 9 m.y.; and southern Diablo Range–southern Sierra Nevada from 9 m.y. to 15 m.y. ago.

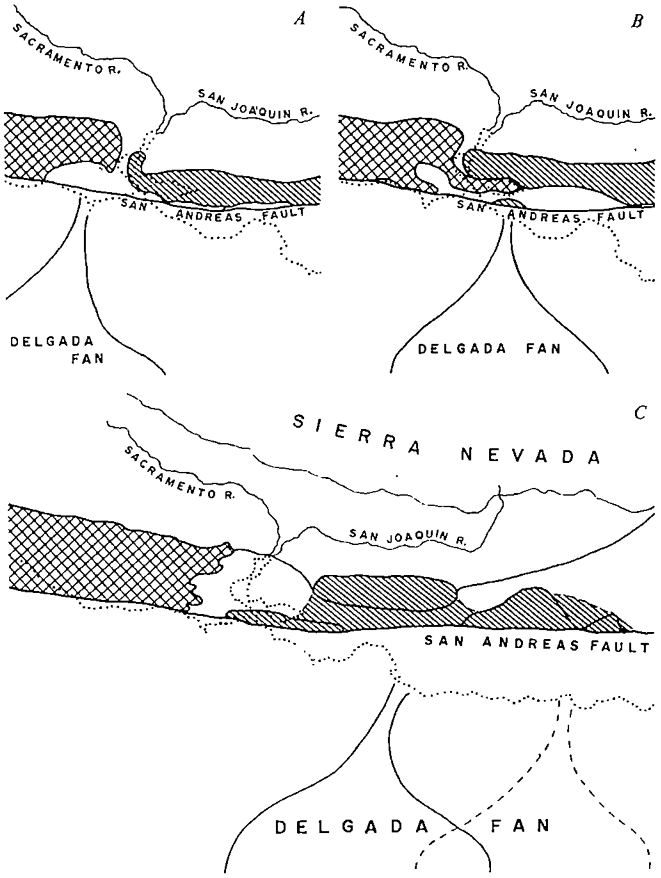

Fig. 1 Palaeogeography of central California[6-8]. Cross-lined represents northern Coast Ranges, lined the Diablo Range and eastern Santa Cruz Mountains, the dotted line is the present coast line. The Sierra Nevada Mountains would be outside the north margin of parts *A* and *B*. *A*, The fan at 4 m.y.; *B*, at 5.5 m.y.; *C*, at 9 m.y. (——) and 15 m.y. ago (- - -).

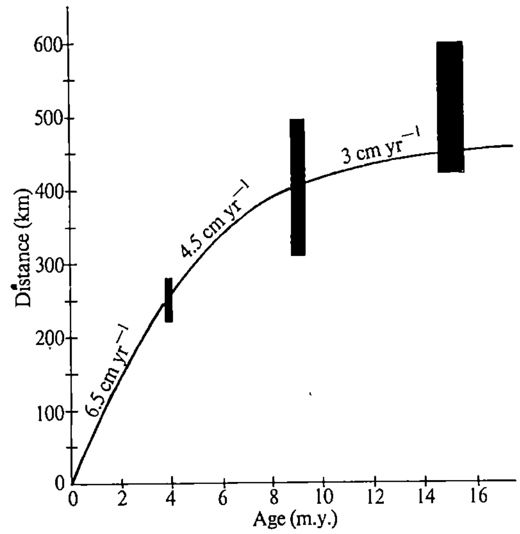

Fig. 2 Increasing rate of motion between California and the Pacific Plate. The ordinate is distance along the San Andreas Fault from the head of Delgada Canyon; the abscissa is absolute age of the fan sediment. The curve represents my preferred interpretation. Shaded areas are possible range of values: 5.5 to 7.0 cm yr^{-1} from Holocene to 4 m.y., 3.4 to 5.5 cm yr^{-1} from 4 to 9 m.y. and 2.8 to 4.0 cm yr^{-1} from 9 to 15 m.y. ago.

The greatest interpretative problem is: how far the fan travelled into a proposed source area before the influence of that source area dominated the fan sediment. The transition from one lithology to another in fan sediment is variable, spanning as little as 200,000 yr at the 4 m.y. change to as much as 1.5 m.y. at the 9 m.y. lithology change. Arbitrarily using the centre point of these time intervals and the palaeogeographic lithologic boundaries allows a preferred interpretation of rates of motion with time between California and the Pacific plate (Fig. 2). In all cases distances to varying lithologies shown in Fig. 1 are measured from the head of Delgada Canyon.

The rate of motion of 5.5 to 7.0 cm yr^{-1} for the past 4 m.y. yielded by this method agrees with the rate calculated from marine magnetic anomalies[3] and adds validity to the choice of space-time boundaries. Reasonable variations in the placement of the palaeogeographic boundaries and possible errors in time boundaries would give ranges of rates of motion shown in Fig. 2. Even if the preferred interpretation is not correct, the data strongly suggest an increase in the rate of motion between California and the Pacific plate from about 16 m.y. to the present.

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Remarkable New Silicate Structure

Pabst, Gross and Alfors[1] described a new hydrated calcium silicate, named rosenhahnite after its discoverer. Lath-like single crystals up to 5 mm long were obtained and the morphology and physical characteristics measured. The composition of the crystals was found to be $Ca_3Si_3O_9H_2O$ with two units in a triclinic unit cell. Thermal dehydration data showed that the molecule of water is given off very slowly at temperatures between 400 and 500° C and a single crystal of rosenhahnite transforms into an almost perfect single crystal of wollastonite, $CaSiO_3$, which is known to contain infinite Si_3O_9 chains. No visible cracking takes place and interfacial angles change little if at all, but the originally clear crystals become opaque and porcellaneous. From density measurements there is apparently about 5% of voids in the converted crystals, but these fissures are not large enough at the surface to admit toluene molecules. The perfect topotactic relation of the two lattices was established (apart from minor details) by the same investigators from partially transformed crystals, which gave almost equally sharp X-ray reflexions from both parts of the specimen.

The transformation to wollastonite is, of course, irreversible (except possibly under high pressure, hydrothermal conditions[1]) and the crystal structure which could explain this transformation posed an intriguing problem as well as promising to throw more light on related materials of importance to cement chemistry. Crystals of rosenhahnite were kindly supplied by Professor Pabst to this laboratory for a structure determination. This has just been completed and the remarkable behaviour of the mineral is, in fact, explained by a remarkable structure.

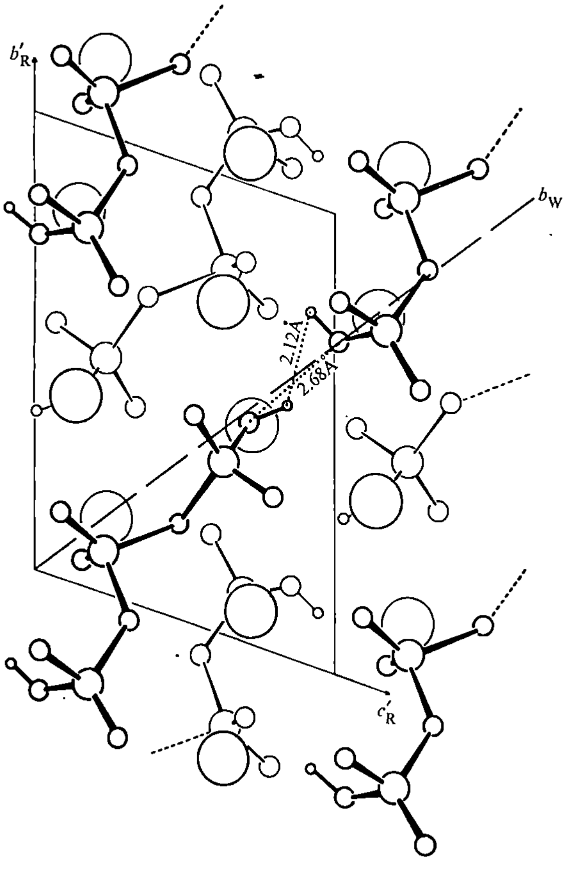

Fig. 1 The structure of rosenhahnite projected on to the plane normal to the a axis. b'_R and c'_R are the projected rosenhahnite axes. The circles, in order of decreasing size, represent Ca, Si, O and H. The direction of b_W, the b axis of the wollastonite into which the crystal transforms on dehydration, is shown by the long dashes. A short dashed line indicates the direction of the bond to the remainder of an incomplete $Si_3O_8(OH)_2$ group. The dotted lines connect the oxygens and hydrogens of a pair of hydroxyls which clearly form hydrogen bonds and almost certainly condense together, liberating a molecule of water, in the polymerization process. All the $Si_3O_8(OH)_2$ groups run nearly parallel to the projection plane.

The structure determination was carried out using over 3,000 independent intensity measurements obtained from a 4-circle diffractometer with MoKα radiation. These intensities were checked against six layers photographed on a Weissenberg camera. A combination of Patterson synthesis and phase determination by direct methods was required to establish the structure. The tetrahedral co-ordination of O round Si was assumed in the early interpretations, but no assumptions were made about the relative arrangements of the tetrahedra or of the Ca atoms. The structure has refined to give a conventional discrepancy index (R-value) of under 4%, using isotropic temperature factors.

The model clearly shows distinct linear (but kinked) groups of three SiO_4 tetrahedra, the two outer silicon-atoms each sharing a common oxygen with the central one. There is no sign of any separate water molecule. One of the three terminal oxygens at each end of the group has a significantly longer bond to Si than the other two and has significant bonding to only one Ca, as against two or three for the others. The only significant peaks in the difference Fourier map occur at just under 1 Å from these oxygen atoms. It is clear that the difference Fourier peaks are the hydrogen atoms, and that OH is attached to each of the terminal silicon atoms. Fig. 1 shows a projection of the structure on the plane perpendicular to the a axis.

The groups of three SiO_4 tetrahedra must be $Si_3O_8(OH)_2$ and the dehydration process consist in the polymerization of these groups into infinite Si_3O_9 chains, each join producing a molecule of water, and local rearrangements giving channels through which these molecules can diffuse.

The determination of the detailed mechanism of the transformation requires an accurate structure of wollastonite. A new set of data has been collected in this laboratory from triclinic wollastonite and the structure refinement is in progress. The results will be reported elsewhere. At present all that can be said is that, from the orientation relationships already established[1], the length of the $Si_3O_8(OH)_2$ groups in rosenhahnite is in the general direction of the b-axis of the wollastonite into which it transforms, and this is the direction of the Si_3O_9 chains.

While the structure and polymerization process have no direct relation to cement chemistry, there is one aspect which may be indirectly relevant. It is now generally agreed that the strength of set cement derives to a considerable extent from physical bonding, but there is some evidence that a significant proportion of chemical bonding may also be present. It has been suggested[2] that chemical bonds might occur if foils or ribbons of the calcium silicate hydrate formed in setting cement came into contact so that the two lattices were aligned. Over a small area "welding" of the two foils might occur. No attempt to calculate the probability of this juxtaposition occurring was made, but it might be expected to be small. However, if a similar process merely required —SiOH groups on the two surfaces to come together, to form a bond by the elimination of water, the probability would obviously be much greater, and greater still if silicate ions were available to help bridge across gaps. Such speculations at least show the possibilities opened up by this exciting new structure.

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Stability of Di-imide

Di-imide, HN=NH, as the prototype azo compound and an isoelectronic analogue of C_2H_4 and O_2, is of great interest to the chemist. It is, however, generally considered to be so unstable as to have only a transient existence at ordinary temperatures[1-3]. Generated *in situ* in aqueous solution, it has been widely used in recent years as a reducing agent[3], but has never been isolated or detected in these systems. It has been detected as a transient in the gas phase in several laboratories. Foner and Hudson[4] produced di-imide by an electric discharge through flowing hydrazine vapour, detected it by mass spectrometry, and showed that it could be trapped at −196° C and regenerated in the gas phase on warming. Trombetti[5], in these laboratories, was able to measure the infrared and vacuum-ultraviolet absorption spectrum of the vapour in a similar flow system, and these two studies seemed to indicate a lifetime of at least a second or two. A brief account by Mock[6] suggests that the lifetime might be much longer; he observed that when di-imide vapour together with ammonia and hydrazine was admitted to the inlet manifold of a mass spectrometer, a signal at $m/e=30$ decayed with a half-life of several minutes and remained detectable for as long as 20 min. Uncertainty and lack of reproducibility of these observations led Mock to conclude only tentatively that di-imide might be as long lived as these data suggest.

We have carried out a detailed study of the chemistry of di-imide, and have found the lifetime in the vapour phase to be surprisingly long, substantially in agreement with Mock's observations. Di-imide was generated by a microwave discharge in hydrazine vapour in a flow system. Hydrazine was trapped out at −78° C, while ammonia and di-imide condensed in a second trap at −196° C, the di-imide forming a ring of bright yellow solid just above the liquid nitrogen surface. The second trap was then isolated, and di-imide, together with about a ten-fold excess of ammonia, could be vaporized by rapid warming and its reactions observed in a static system. The vapour shows a weak "azo" absorption in the near ultraviolet (320–420 nm) which, unlike the spectra of most azo compounds, has a pronounced banded structure. This absorption provided a convenient means of measuring the concentration; Fig. 1 shows a typical decay of di-imide vapour at 30° C measured in this way in a cylindrical spectrophotometer cell 2 cm in diameter and 10 cm long. The decay in this instance was first-order with a half life of 2.4 min. The decomposition of the vapour is reproducible but complex, both in its kinetics and stoichiometry. It depends on pressure and surface, and can follow either first or second-order kinetics depending on conditions. Products of the decomposition are N_2, H_2, N_2H_4 and probably NH_3.

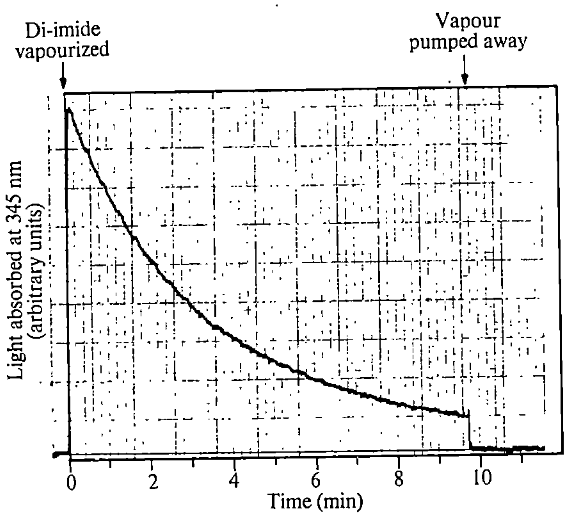

Fig. 1 Absorption of light at 345 nm by di-imide vapour, showing the disappearance with time at 30° C. Initial absorption was about 5%, and initial N_2H_2 pressure probably around 10 torr (an accurate extinction coefficient has not yet been established).

Solid di-imide was found to be very stable, with no appreciable decomposition observed up to the melting point of the solid NH_3-N_2H_2 mixture at −65° C. Di-imide also appeared to persist for many minutes at least in the liquid mixture with ammonia at temperatures between −65° and −30° C.

A detailed account of these studies will be published elsewhere.

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BIOLOGICAL SCIENCES

Ecology of the Ras Muhammad Crack in Sinai

Cracks running through raised Pleistocenic coral reefs form a common environment around the tropical Indian and Pacific Oceans. The cracks can be reached only when they have an opening to the surface of the dry raised reef, and therefore the biota found in the open cracks is a mixture of light-avoiding subterranean species and of shadow-loving marine species. Near the southern tip of the Sinai Peninsula, Cape Ras Muhammad (Fig. 1), an open crack of about 40 m length and 0.20–1.5 m width and about 150 m inland, was discovered in October 1971 (Fig. 2). It is possible, with difficulty, to descend into the crack and dive to depths of over 14 m.

Contact with the sea is proved by the fact that the water level in the crack fluctuates with the tides, and the salinity of the water is about equal to that of the open sea: 23.60 g $l.^{-1}$ against 23.52 in October 1971, and 22.60 g $l.^{-1}$ at the surface and 22.80 g $l.^{-1}$ at 11 m depth against 23.60 g $l.^{-1}$ in the neighbouring lagoon.

The steep and shaded walls of the crack are covered with many algae, among them *Valonia*, *Codium*, *Botryocladia* and calcareous red algae, and sponges, monascidians and terebellid and serpulid polychaets. The fauna is dominated by two species of shrimp. According to Holthuis (personal communication), one is a new species of *Periclimenes*, a transparent pinkish, fairly active species, the other is a new genus of the family

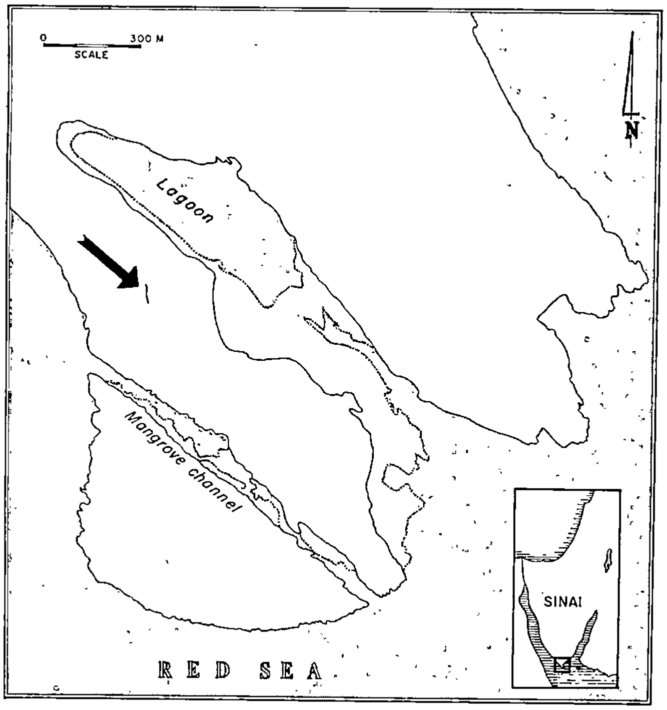

Fig. 1 Cape Ras Muhammad. Arrow points to the site of the "crack".

Hippolytidae, a bright red, blind species. A gobiid was the only fish observed. Swimming above the bottom there are many sphaeromatid isopods. There are large numbers of a *Cardita*-like bivalve, of a very high-shelled keyhole limpet, of an *Acanthopleura*-like chiton and even a few *Spondylus* were found. The sandy sediment accumulated at the shallow northern end of the crack harbours a rich meiofauna including harpacticoids, the ostracod *Bairdia* and tanaidaceans.

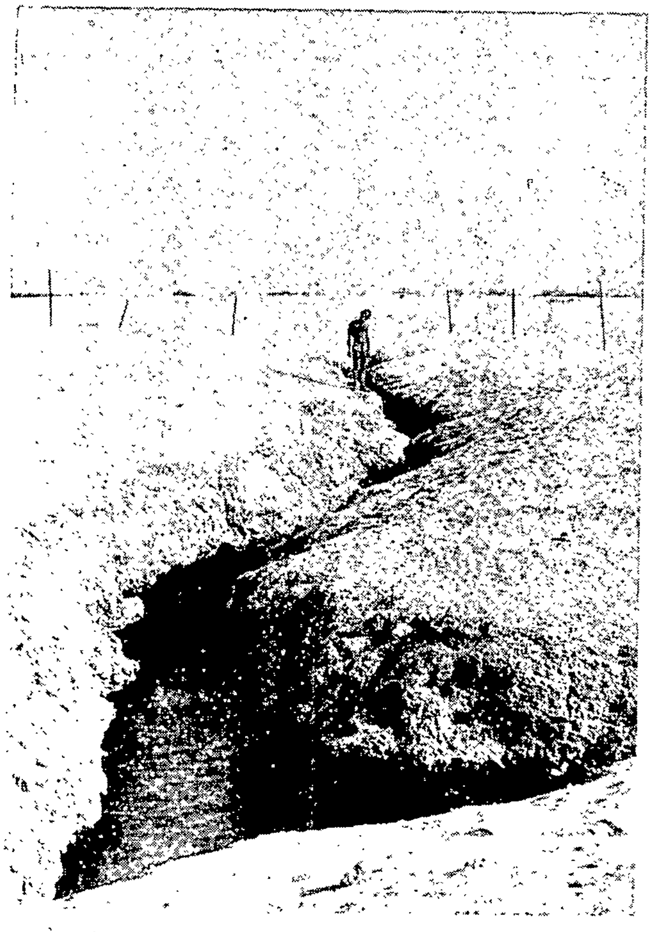

Fig. 2 Southward view of Ras Muhammad Crack.

Most of the inhabitants of the crack must have come through the subterranean connexion with the open sea. Blown-in leaves of turtle grass and crusts of a *Dictyosphaerium*-like alga could supply a second means by which marine animals, or rather their attached eggs, might reach the crack.

Holthuis[1] described this widespread type of environment as "tropical land-locked saltwater pools". Some species typical to this environment are the atyiid shrimp *Antecaridina lauensis* (Edmondson), reported from Devil's Crack (Dahlak Archipelago), Island of Europa and Fiji Islands, or the hippolytid shrimp *Ligur uvae* (Borradaile), reported from Aldabra, Halmahera and Fiji Islands[1]. It was thus not quite unexpected that the same species of the new hippolytide genus of Ras Muhammad recently turned up in collections sent to L. B. Holthuis (personal communication) from Funafuti (Micronesia) and Hawaii. The only reef crack which has been more thoroughly investigated is Devil's Crack on the Island of Entedebir (Dahlak Archipelago, Southern Red Sea)[1-3].

The environment of the coral reef cracks is of worldwide occurrence in the tropics, a new subterranean watery medium in which a change to life in darkness and variable salinity takes place. This recent environment and these distributional patterns may shed some light on the genesis of certain subterranean shrimps, such as the genus *Typhlocaris*, which is represented today by three isolated species around the Mediterranean[4].

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Chromosomal Localization of Human Haemoglobin Structural Genes: Techniques Queried

Price, Conover and Hirschhorn[1] have reported the *in situ* hybridization of haemoglobin mRNA to diploid chromosomes. We think such a conclusion to be impossible because the specific activity of their mRNA was 6×10^{-7} disintegrations per mRNA molecule during the two week exposure of their autoradiographs. As a genome has been reported to contain less than five haemoglobin cistrons[2], even if hybridization and autoradiographic efficiencies were 100%, then at most only 6×10^{-6} silver grains would have been produced over the diploid cell's haemoglobin loci.

They reported up to six grains over the B chromosomes after a two week exposure and it is difficult to believe that these grains were due to specific mRNA hybrids. From their data in Fig. 1, the specific activity of their mRNA was 5 c.p.m. μg^{-1}. Wimber and Steffensen[3] used 5S RNA at 4×10^6 d.p.m. μg^{-1} and after *in situ* hybridization to *Drosophila* polytene chromosomes, they detected only 20 grains per month over the 5S band. Such a band contains 200 (redundancy) × 1,000 (polyteny) × 2 (diploidy) = 400,000 cistrons. One can easily see why the mRNA of Price *et al.*[1] was not radioactive enough to detect mRNA cistrons in a diploid chromosome even if the haemoglobin locus is a million-fold redundant.

We also suggest that instead of selecting eight cells out of 1,000 for analysis, one should show the frequency distribution of grains over as many of the cells as is practical. The unlabelled cells are as valid an experimental sample as the presumably "labelled" ones and excluding them from the analysis is a biased sampling procedure. A bacterial ^{3}H-RNA control and a poly A competition are also necessary for proper analysis of these results.

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Do Bacteria Have a Nuclear Membrane?

The idea of Stanier and van Niel[1] that bacteria (and possibly blue-green algae) are "prokaryotic" organisms, lacking a nuclear membrane, appears to have been accepted almost without argument. All other cells possess such a membrane, and are "eukaryotic", according to this theory.

The inner layer of the bacterial cell envelopes, however, which is commonly regarded as comparable with the semipermeable membrane of other cells, carries the attachments of the flagellum and the nuclear system. In "eukaryotic" protista it is with the nuclear membrane that such structures are associated[2].

Bacterial murein[3] has been described[4] in this journal as a layer between the cell wall proper and the cytoplasmic membrane; "the meat in the sandwich", which most appropriately consists of a lipoprotein complex. Although this may, and probably does, differ in chemical detail from the composition of classical cell membranes, and it is not alike in all bacteria, above the membrane, which is performing two of the most important known functions of the primitive nuclear membrane, there is a structure that, in some cases, at least chemically, suggests a membrane more than a cell wall, and could fairly be regarded as having been evolved from a previously existing, semipermeable membrane.

I suggest on the basis of general morphological relationships[5] that the structure which now represents the cell membrane of bacteria may have originated in the nuclear membrane of an ancestral form; with the corollary that the murein layer could be derived from the cell membrane, the functions of which had been taken over by the nuclear membrane. The differences which may now exist between the composition of these organs, and that of their hypothetical forerunners, are no greater than those of many comparable examples, in the wider field and longer scale of evolution (for example, the retinal rods from cilia).

There is no reason to presume that bacteria, because of their small size, are in any way primitive[6]. They are, indeed, highly specialized organisms, making use of their small size, and consequent low bulk-surface ratio and rapid metabolism. They are almost certainly derived from other, more primitive, flagellate protista, and the origins of their organs must be sought in the general structural pool.

This hypothesis gives rise to further questions; the most obvious of these is: what service is such a transformation, whereby the cell membrane reinforces the wall, while the nuclear membrane takes over its function? The best available answer refers back to the advantages of a small size and a large surface area, as the latter can be maintained, against the relatively strong forces of surface tension, in an already exceptionally small cell, only by great rigidity in the cell envelopes.

It may be that the supposed resemblance between bacteria and blue-green algae in having no nuclear membrane will prove to be as invalid as the previous theory; that they were alike in having no nucleus at all. They are alike mainly in their small size, and in the convergent adaptations that this produces. Positive groupings, based on negative criteria, are seldom durable in biology, and separate creation, even of organs, must have some evolutionary background.

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Can Mitochondrial Complementation be Used as a Tool in Breeding Hybrid Cereals?

Several papers[1–6] have been published in which it is claimed that mitochondrial heterosis and mitochondrial complementation are related to the yield potential of F_1 hybrid cereal cultivars. Mitochondrial heterosis is measured by the superior oxidative and phosphorylating efficiency of mitochondria isolated from heterotic F_1 hybrid cultivars when compared with those isolated from the corresponding parental cultivars. Although these parameters can be measured only after a small quantity of F_1 hybrid seed has been produced they may prove useful to plant breeders as a preliminary appraisal of the yield potential of an F_1 hybrid before undertaking extensive field trials.

Mitochondrial complementation is a more complex phenomenon, reported to occur when mitochondria isolated from the two prospective parents are mixed *in vitro*. The phenomenon can be recognized by the superior biochemical activity (measured by the rate of oxidation and efficiency of phosphorylation) of a 1 : 1 mixture of the mitochondria of the two potential parents over the arithmetic mean of the two preparations when assayed separately. Sarkissian and Srivastava[7] claim that there is a correlation between mitochondrial complementation and mitochondrial heterosis in F_1 hybrid maize cultivars and have extended their observations to include F_1 hybrid wheat[3]. Mitochondrial complementation is therefore a potentially much more useful tool in plant breeding programmes than mitochondrial heterosis because it would predict, without first producing the hybrid, which cultivars, when crossed, would yield heterotic F_1 hybrids.

McDaniel[6] reiterates that both mitochondrial heterosis and complementation can be used to predict the relative yield potentials of F_1 hybrid barley cultivars. He states that use of mitochondrial complementation "should provide a more efficient and rapid method of screening potential breeding material and evaluating hybrids". However, McDaniel does not discuss the relative merits of complementation and heterosis to the plant breeder, nor does he distinguish between the phenomena of heterosis and complementation in his correlation of mitochondrial data with yield data and, therefore, does not provide convincing evidence that either phenomenon alone is correlated with yield potential.

Before incorporating mitochondrial complementation tests routinely into any breeding programme it is necessary to assess the technique for its reproducibility and reliability, and our investigation has had this as its primary objective. Initial tests were carried out using the barley cultivars 18–17 and Arivat, as McDaniel reported[4] that mixtures of mitochondria obtained from these two cultivars gave an increase in ADP : O ratios of 22%. In a standard experiment we extracted mitochondria from twenty barley scutella with embryonic axes from seeds germinated for 18 h at 27° C. The tissue was homogenized in a chilled pestle and mortar for one minute in 5 ml. of isolating buffer. The resultant brei was filtered through nylon mesh and the filtrate centrifuged at 2,000*g* for two minutes to remove starch and cell debris. We sedimented the mitochondria by centrifugation at 30,000*g* for three minutes, and further separated the mitochondria from residual starch by pouring off the supernatant, adding 3 ml. of washing buffer, rotating the tube through 180° in the rotor, and centrifuging at 6,000*g* for one minute[8]. The mitochondrial pellet was then suspended in 0.1 ml. of assay buffer. The buffer solutions with which we isolated, washed and assayed the mitochondria were as described by McDaniel[4] except that 0.1% of fatty acid free bovine serum albumin was added to all three. The rate of oxygen uptake and ADP : O ratios were measured using conventional polarographic techniques with a total assay volume of 0.3 to 0.5 ml. Using this method mitochondria were obtained with respiratory control ratios of between 3.0 and 5.0. Although the ADP : O ratios were low, they were of the same order as those quoted by McDaniel (Table 1).

Preliminary replicated control experiments indicated the need for a high degree of precision at every stage of the procedure as a prerequisite to reliable data, necessary if the technique is to be used in a large scale selection programme. The consistent production of uniform pellets of mitochondria was largely achieved by producing mitochondria from both parents and the 1 : 1 mixture simultaneously in one "preparation". The basic experimental design used was a 3×3 Latin square in which the mitochondria from each cultivar were assayed in each of the three "preparations". Within successive "preparations", the mitochondrial pellets of the three cultivars were assayed in rotation to eliminate bias due to ageing. No complementation could be detected using this technique (Table 1, experiment *B*). Many modifications were tried as listed in Table 1 but it was not possible to obtain any mitochondrial complementation statistically significant at the 5% level in either the ADP : O ratio or any other parameter of mitochondrial activity.

A similar series of experiments was carried out using the wheat cultivars 31 MS and 28, in which Sarkissian and Srivastava report[3] finding levels of mitochondrial complementation of up to 54%. In our initial experiment H the technique described by Sarkissian and Srivastava[3] was used, but in later experiments I to L the modifications listed in Table 2 were made as recommended by Sage and Hobson (private communication). It is apparent from data in Table 2 that under no conditions were we able to detect statistically significant levels of complementation.

Table 1 Statistical Analysis of Mitochondrial Complementation in Barley Cultivars 18–17 and Arivat

Exp. No.	18–17 ADP : O mean	1 : 1 Mix ADP : O mean	Arivat ADP : O mean	MC obtained	Sig. at 5% level	Least MC detectable at 5% level
A	2.08*	2.44†	1.92*	+22.0%	—	—
B	1.61*	1.68*	1.70*	+1.5%	N.s.	±8.7%
C	1.47*	1.54*	1.62*	−0.6%	N.s.	±8.7%
D	1.84*	1.84*	2.00†	−4.5%	N.s.	±5.2%
E	1.23*	1.26*	1.39†	−4.3%	N.s.	±9.9%
F	1.62*	1.61*	1.72*	−3.7%	N.s.	±9.0%

The substrate was α-oxoglutarate (12 mM in experiments *B*, *C* and *D* and 10 mM in experiments *E* and *F*). Means of ADP : O ratios with different (*, †) superscripts, within each experiment, are significantly different at the 5% level. Mitochondrial complementation is calculated by the expression:

$$\mathrm{MC} = \frac{\mathrm{ADP:O\ (1:1\ mix) - ADP:O\ (MP)}}{\mathrm{ADP:O\ (MP)}} \times 100$$

where the mid-parent value, ADP : O (MP), is derived from ½ADP : O (18–17)+½ADP: O (Arivat).

Experiments *A* to *F* were carried out with the following modifications:

A, McDaniel's data[4].

B, The techniques described in the text were used.

C, The fast isolation procedure was replaced by a slow method, comprising spins of 1,000*g* (5 min) and two of 10,000*g* (each 10 min). Furthermore, BSA was omitted from all solutions, and NAD and TPP omitted from the assay buffer solution.

D, Seed samples of 18–17 and Arivat, used in experiment *A*, were obtained from McDaniel and analysed as in experiment *B*.

E, The germination time for the barley seedlings was increased to 30 h, and mitochondria isolated by the slow procedure. Six replicates of each genotype were prepared individually, thereby dispensing with the Latin square.

F, The 1 : 1 mixture was prepared from pellets of isolated mitochondria in a randomized double 3×3 Latin square, but otherwise the technique was as described in the text.

Table 2 Statistical Analysis of Mitochondrial Complementation in Wheat Cultivars 31 MS and 28

Exp. No.	31 MS ADP : O Mean	1:1 Mix ADP : O Mean	28 ADP : O Mean	MC obtained	Sig. at 5% level	Least MC detectable at 5% level
G	3.8	5.4	3.2	+54.3%	—	—
H	1.81*	1.82*	1.78*	+1.3%	N.s.	±10.3%
I	2.07*	2.23†	2.23†	+3.9%	N.s.	±5.6%
J	2.28*	2.40*	2.41*	+2.3%	N.s.	±7.7%
K	2.15*	2.23*†	2.30†	+0.3%	N.s.	±5.6%
L	2.10*	2.03*	2.20*	−5.8%	N.s.	±8.4%

In experiments *G* and *H* the substrate was α-oxoglutarate (10 mM).

In experiments *I*, *J*, *K* and *L* the substrate was α-oxoglutarate (10 mM) with malonate (5 mM).

Means of ADP : O with different (*, †) superscripts, within each experiment, are significantly different at the 5% level.

Mitochondrial complementation (MC) is calculated as given in Table 1.

Experiments *G* to *L* were carried out with the following modifications:

G, Sarkissian and Srivastava's data[3].

H, The techniques described by Sarkissian and Srivastava[3] were used in the context of a randomized double 3×3 Latin square.

I, The composition of the buffer solutions was modified as recommended by Sage and Hobson. The isolating and washing buffer comprised sucrose (0.45 M), BSA (0.075%), EGTA (2 mM), TES (1 mM), $MgCl_2$ (1 mM) and potassium phosphate (67 mM, *p*H 7.2), and the assay buffer was changed to mannitol (0.3 M), KCl (10 mM), $MgCl_2$ (5 mM), EGTA (2 mM), TES (10 mM), BSA (0.075%) and potassium phosphate (10 mM, *p*H 7.2).

J, The time of isolation of mitochondria was reduced from 15.0 min to 12.5 min.

K, The operators were given coded materials to eliminate personal bias.

L, The type of fabric used by Hobson for filtering the wheat shoot brei was used, and the concentration of mitochondrial protein in the assay buffer solution was raised from about 0.6 mg $ml.^{-1}$ to 0.75 mg $ml.^{-1}$. In Experiments *I* to *L* each genotype determination was replicated six times in individual preparations at random, as in *E*.

The reason for the discrepancy between this data and that reported from other laboratories cannot as yet be defined. The final column in Tables 1 and 2 quotes the minimum levels of mitochondrial complementation significant at the 5% level which could have been detected in our experiments, calculated from each respective error term. Clearly levels as large as those quoted by McDaniel, Sarkissian and Srivastava could be detected, as well as the low level of +9% found by Sage and Hobson with wheat cultivars Peko and Cappelle Desprez.

The divergence apparently lies in an undefined detail of procedure, despite frequent and exhaustive discussions with each group of workers. One notable point of interest, however, is the relatively large differences in the ADP : O ratios, particularly with wheat, obtained by the different groups. The ADP : O ratios quoted in this paper (2.2) are lower than those obtained by Sarkissian and Srivastava (3.0–6.0)[3] and Sage and Hobson (3.0). We suspect that further investigation of this discrepancy will eventually help to resolve the controversy concerning mitochondrial complementation.

The conclusion from our investigations is that we have been unable to demonstrate mitochondrial complementation, despite paying careful attention to published procedures. Until the phenomenon is better understood and the experimental conditions necessary for its expression more accurately described, we cannot, at present, recommend that mitochondrial complementation be used in a hybrid cereal breeding programme.

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An Increasing Fitness Function for a Population with Many Niches

THE mean viability, V, increases from generation to generation[1–3] for a single autosomal locus with multiple alleles. Ewens[4] has recently proved that for an arbitrary number of linked loci, with viability additive over loci, mean viability is again increasing. This latter result was proved using the former.

Here I show a further case in which a fairly simple fitness function increases from generation to generation. Levene[5] formulated a model in which there were a number, m, of niches. Mating was at random amongst the total population, the resultant offspring migrating to the niches, which were of relative size c_i, and being subject to selection in those niches.

In a population in which there are n alleles A_j $(j=1, 2, \ldots n)$, and the viability of the A_jA_k genotype in the ith niche is a_{ijk}, p_j is the frequency of the jth allele just before mating, and p_j' is the frequency one generation later, then[6]

$$p_j' = \sum_{i=1}^{m} \sum_{k=1}^{n} \frac{c_i a_{ijk} p_j p_k}{V_i}$$

where $V_i = \sum_{j=1}^{n} \sum_{k=1}^{n} a_{ijk} p_j p_k$, the mean viability in the i^{th} niche.

Writing $V = \sum_{i=1}^{m} V_i^{c_i}$ we obtain

$$p_j' = \frac{p_j \, \partial V / \partial p_j}{\sum_{j=1}^{n} p_j \, \partial V / \partial p_j} \cdot \qquad (1)$$

Equation (1) is essentially equivalent to that studied by Baum and Eagon[7]. They demonstrated that $V' \geq V$, with equality only at an equilibrium of the system, that is, when $p_j = p_j'$ for all j. Thus the fitness function V increases from generation to generation. In this case V is considerably more complicated than in the single niche problems, and the possibility arises of several equilibria or of continuous curves of equilibria existing[6]..

We should note that all the cases of increasing fitness mentioned above, and also the p-sex model case of Blakeley[8] are direct, or indirect, consequences of the same theorem[7]. All these models have certain basic features, first, random mating amongst the whole population, and second, identical viabilities for the two sexes. The addition of extra complexity such as inbreeding, differential selection for males and females, or asymmetry of genetic system destroys the property of increasing V.

Finally we note that the various systems with increasing V can be combined; V will increase for selection with n alleles, m niches, k loci with additive fitness for loci, and p sexes.

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Depression of Yield in Ryegrass Exposed to Sulphur Dioxide

PREVIOUS work[1] has shown that substantial economic losses may occur when S23 ryegrass is grown in areas of high coal-smoke pollution. Evidence suggested that sulphur dioxide was the toxic factor producing the depression in yield, although this could not be proved. We decided to investigate the effects of prolonged periods of low SO_2 concentration on the growth of S23 *Lolium perenne* in order to establish whether SO_2 can cause invisible injury and also to measure the depression of yields at different concentrations of the gas. We also used clones of wild *L. perenne* collected from Helmshore in a polluted region of East Lancashire. Observations at the ADAS Experimental Husbandry Farm at Helmshore have indicated that the native ryegrass in the district is apparently tolerant to the polluted atmosphere (C. H. Mudd, personal communication).

We grew the plants in bowls inside two Perspex chambers situated in an open-sided greenhouse. The chambers were ventilated with the ambient air, which was purified by passage through activated charcoal, followed by an absolute filter. A controlled uniformly distributed concentration of sulphur dioxide was maintained in one chamber, by bleeding SO_2 at a controlled rate into the air inlet pipe. The plants were grown in a well fertilized brown earth, watered by sub-irrigation.

Table 1 Final Yield of S23 *Lolium perenne* Grown for Nine Weeks in 343 μg m^{-3} or 14 μg m^{-3} SO$_2$

	No. of tillers	No. of living leaves	No. of dead leaves	Dry weight living leaves, g	Dry weight "stubble", g	Dry weight dead leaves, g	Leaf area, cm^2
SO$_2$ plants	5.95±0.66	19.59±1.96	6.64±0.18	0.175±0.016	0.082±0.008	0.042±0.001	94.4±9.0
Control plants	10.20±0.33	34.02±1.19	4.56±0.23	0.324±0.012	0.155±0.008	0.023±0.002	168.6±4.6
Decrease in productivity of SO$_2$ plants below controls	41.7%	43.0%	45.6% increase over control	46.1%	46.9%	79.3% increase over control	44.0%
P=	<0.001	<0.001	0.02–0.05	<0.001	<0.001	<0.001	<0.001

Means per plant with standard errors shown.

Nine bowls in each chamber were sown with S23 seed and thinned out to sixteen plants per bowl; six bowls per chamber were planted with sixteen uniform tillers from two Helmshore clones. The SO$_2$ concentration inside each chamber was monitored for weekly periods throughout the experiments, using the standard titration method[2] and the accuracy of the technique was checked by regular sulphate analyses of the hydrogen peroxide solution.

In the first experiment the S23 seeds were sown and the Helmshore tillers planted on 3.8.71. The experiment continued for nine weeks and the mean SO$_2$ concentration was 343 μg m^{-3} (0.120 p.p.m.) in the polluted chamber and 14 μg m^{-3} (0.005 p.p.m.) in the control. A non-destructive growth analysis was carried out after five weeks, when the numbers of leaves, numbers of tillers, and the length of the third leaf on each S23 plant were determined. This indicated decreases in yield of the plants exposed to the higher SO$_2$ concentrations, of 13% in leaf number, 22% in tiller number and 8% in the length of the third leaf.

At the termination of the experiment the S23 plants in the polluted chamber were much smaller than those in the control chamber; they were also rather chlorotic in comparison with the controls, which looked healthy. Living leaves, dead leaves and tillers were counted on each plant and the dry weights determined for living leaf blades, dead leaf blades and the remaining "stubble"; leaf areas were also determined.

A reduction in yield of about 46% occurred in the polluted chamber S23 plants in comparison with the S23 plants grown in the control chamber (Table 1). This was due to a decrease in leaf and tiller production and also by an increase in the rate of senescence of the leaves; this is in agreement with the findings of Bleasdale[1]. The reduced number of leaves on the SO$_2$ plants was primarily the result of lower leaf production rather than the increased rate of senescence.

For the Helmshore plants no significant difference was found in the productivity of either clone between the two treatments, except that more dead leaves were present in the control chamber although the dry weight was the same in each case; they also showed a healthy green appearance in both chambers.

A second experiment was carried out with the role of the control and polluted chambers reversed to show that the depression in yield in the first experiment was not caused by slight differences between the chambers. The experiment was carried out over the winter with the mean SO$_2$ concentration lowered to 191 μg m^{-3} (0.067 p.p.m.) which is within the range of mean winter SO$_2$ levels reported from polluted rural areas[3]. The experiment commenced on 12.10.71 and terminated on the 10.4.72, a total of twenty-six weeks. Growth occurred slowly throughout most of the winter, but increased rapidly during the warm weather in March and early April.

Six weeks after sowing, when the plants were mostly at the 3-leaf stage, the productivity of the S23 was examined by measuring the length of the second leaf. This indicated a slightly but significantly better growth in the polluted chamber. Sixteen weeks from sowing another non-destructive growth analysis was carried out on the S23 plants, counting numbers of living leaves, dead leaves and tillers. The results indicated a depression in plants exposed to SO$_2$ of 27% in living leaf number and 41% in tiller number and an increase of 75% in the number of dead leaves.

The results of the final harvest are shown in Table 2. The dry weight of the shoots of the S23 plants in the polluted chamber was depressed by 52% in comparison with the controls, this being accounted for by a depression in leaf and tiller formation and an increased rate of leaf senescence. No significant difference was found between treatments in the dry weights of the shoots of the Helmshore plants.

Many aspects of the problem have still to be investigated. Differences in wind speed may have an effect in that a higher speed will decrease r_a, the aerodynamic resistance, and hence increase the dose of SO$_2$ to the surface of the plant; plants growing under field conditions with higher wind speeds than in the experimental chambers might react in a different manner to SO$_2$ pollution, as a result of the combined effects of wind and SO$_2$. The results indicate that SO$_2$ depresses yields under both summer and winter conditions, but further investigations are necessary to determine the relative importance of SO$_2$ in the ambient air at different seasons. Another important factor is the possible ameliorating effect on SO$_2$ damage of increased levels of nitrogen fertilizers, which will be investigated in the next stage of this work. In spite of the limited extent of this preliminary work, we feel that the results so far suggest that SO$_2$ concentrations typical of polluted districts can seriously depress the yield of S23 *Lolium perenne*. It is possible that the native population in polluted districts has been selected for tolerance to SO$_2$ pollution and this opens up possibilities for breeding tolerance into commercially available varieties. It is difficult to say whether or not invisible injury has occurred; the polluted plants were somewhat yellow, but this

Table 2 Final Yield of S23 *Lolium perenne* Grown for Twenty-six Weeks in 191 μg m^{-3} or 9 μg m^{-3} SO$_2$

	No. of tillers	No. of living leaves	No. of dead leaves	Dry weight living leaves, g	Dry weight "stubble", g	Dry weight dead leaves, g	Leaf area, cm^2
SO$_2$ plants	14.84±0.67	47.31±2.31	12.02±0.55	0.388±0.021	0.217±0.014	0.047±0.003	203.6±13.2
Control plants	25.18±0.77	85.61±2.35	6.39±0.39	0.791±0.026	0.478±0.019	0.027±0.003	417.2±18.0
Decrease in productivity of SO$_2$ plants below controls	41.1%	44.7%	88.1% increase over control	50.9%	54.6%	77.7% increase over control	51.2%
P=	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Means per plant with standard errors shown.

might not be noticed in the field in the absence of an adjacent control.

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Crystallization *in vivo* of Rhabdophane in Human Lungs

WE have observed an unusual accumulation of inorganic rod-like particles with a mean diameter of about 10 nm in the lungs of two reproduction photographers (Fig. 1). From the electron diffraction of the particles the *d*-spacings were calculated (Table 1).

The X-ray powder diffraction pattern of the isolated lung dust does not show any additional lines except those of quartz which can be traced in every human lung. A semiquantitative X-ray fluorescence analysis showed the presence of the following elements (in order of decreasing frequency): cerium, lanthanum, calcium, neodymium, thorium, praseodymium, yttrium and samarium. In addition; silicon, iron and potassium, which are common in lung tissue, were also detected. Peaks at 1,060 cm^{-1}, 623 cm^{-1} and 540 cm^{-1} in the infrared spectrum indicate that the rare earth elements are combined with phosphate ions.

These results leave no doubt that the particles consist of rhabdophane, (La, Ce, Nd . . .) $PO_4 \cdot H_2O$, or at least partly of the rather rare thorium-rich variety brockite. The analysis of the elements contained in the ash of a arc-lamp electrode which had been used in the workshop where both photographers had worked showed a pattern similar to the lung dust with respect to the rare earth elements. X-ray powder diffraction analysis revealed, however, that in the ash these elements were present as oxides. Therefore, it must be concluded that the inhaled oxides were gradually converted to rhabdophane (or brockite) within the lung tissue. To our knowledge the *in vivo* crystallization of these rare minerals has not been previously observed.

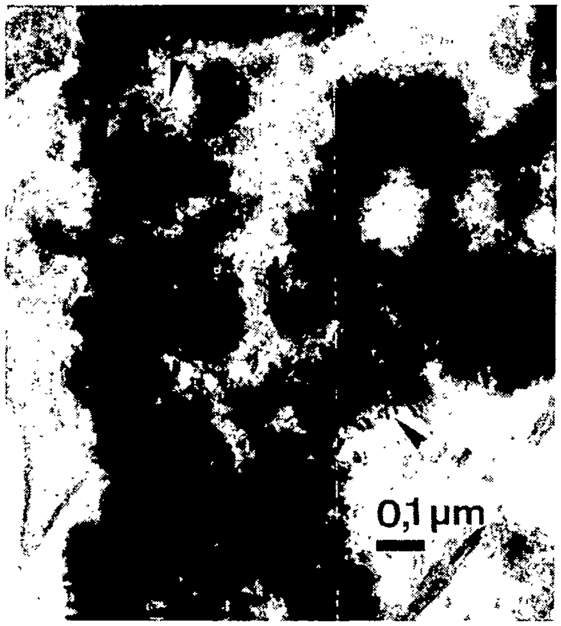

Fig. 1 Electron micrograph of lung tissue: detail of a rhabdophane containing cellular inclusion body.

Table 1 Electron Diffraction Pattern of Lung Dust and *d*-Spacings of Rhabdophane and Brockite

Lung dust		Rhabdophane (ASTM 12–277)		Brockite (ASTM 15–248)		
d (Å)	I/I_0	*d* (Å)	I/I_0	*d* (Å)	I/I_0	*hkl*
6.08	30	6.07	60	6.06	40	100
4.39	60	4.40	80	4.37	70	101
3.53	50	3.49	60	3.47	50	110
3.04	90	3.02	100	3.03	100	200
2.82	100	2.83	80	2.83	70	102
2.36	20	2.36	40	2.37	30	112
2.12	40	2.15	80	2.15	70	211
1.93	20	1.92	40	1.92	30	301
1.86	40	1.859	60	1.86	50	212
Hexagonal		Hexagonal		Hexagonal		
$a_0=7.02$		$a_0=6.98$		$a_0=6.98$		
$c_0=6.35_5$		$c_0=6.39$		$c_0=6.40$		

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Dimethylnitrosamine in the Human Vaginal Vault

THE high frequency of cancer of the uterine cervix in southern Africans[1] and the general epidemiological features of the disease[2] suggest that chemical carcinogens might be found in infected discharge from the human cervix.

Pathological cervical and vaginal discharges contain cellular matter in various stages of degradation in a "protected" environment at *p*H (about 5.5), and temperature favourable for chemical change. Discharges are usually infected with a wide variety of microorganisms, often including *Trichomonas*, *Monilia* and *E. coli.* Nitrosamines, well known potent carcinogens[3], might be synthesized by such organisms or formed when and where amines and nitrites (or possibly nitrates in reducing conditions) are present.

Samples were prepared and dimethylnitrosamine isolated by the technique of Nunn and Du Plessis[4]. Isolation and identification of nitrosamines in biological samples (especially when present in the p.p.b. range), based on final gas chromatograph-mass spectrometry, are the most reliable (L. S. Du P. and J. R. N., in preparation). Our identification of dimethylnitrosamine was based both on gas chromatography (where a peak coincided with that of dimethylnitrosamine under two different sets of conditions) and on the mass spectrum of the component responsible for this peak. This spectrum displayed distinctive peaks at mass 74 (parent ion of dimethylnitrosamine) and at mass 30, which could only have been due to NO^+, characteristic of nitrosamines. Although the increased intensity of mass 30 could have been due to an ion such as $^{15}N_2^+$, it is extremely unlikely here.

A detailed examination was made of pooled discharges taken from 100 African patients attending an antenatal clinic in Johannesburg. Specimens were collected at random, the criterion of choice being only the availability of material. Most patients in this first series were pregnant, because the physiological (and pathological) secretion from the endocervix is quite profuse. Specimens were taken almost exclusively from patients at their first visit. Apart from overt bleeding, cases with cervical pathology were not excluded, but these probably accounted for only a very small proportion of those examined. Most could be termed "physiologically normal" cases.

Samples (about 0.2 to 0.5 ml. from each patient) were taken by bulb and Pasteur pipette. A sterile 'Tampax' outer insertion tube (the cardboard outer sleeve) was inserted into the axis of the vagina and the posterior vaginal wall was visualized. The pipette was then inserted, the contents of the posterior fornix aspirated by gentle suction from the bulb, and the tube discarded. Empty pipettes were used as control checks and during analysis were treated identically to the test pipettes. Each pipette was placed in a clean glass tube, which was sealed with a stopper and stored at low temperature. Distilled water (4 ml.) was added to each of the control and test collection tubes; the test ones were manipulated to ensure proper dispersal of the discharge material from the pipette into the water. The water in each test and control tube was then frozen by gentle mixing of the tube while immersed in liquid air. Tubes (without any grease on ground joints) were then freeze-dried. The distillate (about 30 ml.) was collected in a single collection flask and extracted with dichloromethane (4 × 3 ml.) after thawing. The organic phase was separated each time by pipette. The combined dichloromethane extracts (about 50 ml.) from the distillation of 36 tubes (100 test samples) were dried over $Mg(ClO_4)_2$ and concentrated to about 300 μl. in a flask fitted to a vacuum jacketed Vigreaux column.

Chromatography of this solution revealed a number of peaks, one of which was coincident with that of dimethylnitrosamine (retention time 3.2 min). No peaks were detected when control materials were analysed by identical gas chromatography; the test extract was therefore further examined in a gas chromatograph-mass spectrometer linked system ('Pye-Unicam' gas chromatograph and an 'A.E.I. MS30' mass spectrometer) under carefully specified conditions.

One of the peaks in the gas chromatogram (shown by the total ion monitor) again coincided exactly with that given by dimethylnitrosamine (retention time 68 s) under the same conditions. The mass spectrometer was set to scan at 10 s per decade. Blank—that is, "background"—mass spectra were recorded at the retention time of dimethylnitrosamine after the injection of pure dichloromethane into the gas chromatograph. A series of mass spectra was recorded across the peak in question (25 μl. injection of the dichloromethane extract). The maximum intensity of mass 74 was 148 units, as compared with a background intensity of 12 units, a twelve-fold increase. Concurrently, mass 30 (NO^+) doubled in intensity from 11 to 22 units.

We suggest these results indicate the probable presence of dimethylnitrosamine in pooled specimens of human cervical and vaginal discharge matter; no attempt has been made to estimate the actual amounts present.

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In vitro Fertilization of Rat Eggs

AFTER the recognition of "capacitation of sperm" by Austin[1] and Chang[2], successful *in vitro* fertilization of mammalian eggs was achieved in many species[3-17]. Although fertilization of rat eggs *in vitro* has been attempted[1,18-20], incorporation of sperm into the vitellus was observed only after the dissolution of zona pellucida by chymotrypsin[19]. Here we report fertilization of intact rat eggs *in vitro* and the results obtained.

Mature female CD strain rats were kept in a constant temperature room (23–25° C) with artificial light (19.00–7.00 h darkness) and their vaginal smears inspected daily. As ovulation usually occurs at about 2.00 h on the pro-oestrous to oestrous night[21], the eggs were considered to be about 4 to 5 h and 7.5 to 8.5 h after ovulation when pro-oestrous rats were killed at 6.00 to 7.00 and 9.30 to 10.30 h respectively on the next day. Superovulation of mature rats was performed by

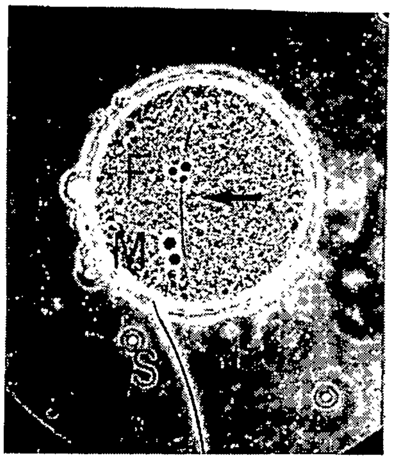

Fig. 1 A rat egg at pronuclear stage, fertilized *in vitro*, showing male pronucleus (M), female pronucleus (F), the fertilizing sperm tail (arrow) and a sperm attached to the zona pellucida (S). Photographed before fixation under a phase-contract microscope. Sperm for insemination were prepared either from the cauda epididymis or from the uterus of a female mated 0.5 to 1 h, or 10 to 11 h, previously. A drop of dense sperm mass was put into a watch glass and covered with 3 ml. of medium (modified Krebs-Ringer bicarbonate solution containing 114.2 mM NaCl, 4.78 mM KCl, 1.71 mM $CaCl_2.2H_2O$, 1.19 mM KH_2PO_4, 1.19 mM $MgSO_4.7H_2O$, 25.07 mM $NaHCO_3$, 0.55 mM sodium pyruvate, 21.58 mM sodium lactate and 5.55 mM glucose, to which 4 mg ml.$^{-1}$ of crystalline bovine serum albumin, 50 μg ml.$^{-1}$ of streptomycin sulphate and 75 μg ml.$^{-1}$ of penicillin G (potassium salt) were added). The *p*H value of the medium was adjusted to 7.4 to 7.5 by addition of 1 M NaOH and the final solution was filtered through a millipore filter to ensure asepsis. Blood of female rats was collected by heart puncture, allowed to clot and then centrifuged. Serum was sterilized by filtration through a millipore filter and stored under paraffin oil at 2 to 5° C for no longer than five days. The uterine fluid was collected from oestrous rats by means of a syringe needle. Insemination was performed by adding 0.4 ml. of the sperm suspension to the egg clot under the oil, after removing oviducts and débris. In some cases the egg clot was washed three times with the same medium to remove the oviducal fluid. After adding 0.1 or 0.2 ml. of heated rat serum (at 56° C for 40 min), the eggs and sperm were thoroughly mixed and incubated at 37° C in an atmosphere of 5% CO_2 in air. The final concentration of sperm in the suspension was 1,000 to 4,000 sperm mm^{-3}.

i.p. injection of 30 IU of pregnant mare's serum (PMS) on the morning of oestrus and 30 IU of human chorionic gonadotrophin (HCG), 52 to 58 h later; the rats were killed 14 to 16 h after injection of HCG. Oviducts were placed under light paraffin oil, equilibrated with 5% CO_2 in air in the presence of a small volume of saline, in a watch glass kept at 37° C and the eggs in cumulus clot were released by dissecting the ampular portion of the oviducts. Sperm for insemination were prepared . The eggs were inseminated with sperm prepared as in Fig. 1.

After incubation for 8 to 12 h, the eggs were removed, mounted on a slide and examined. They were then fixed with neutral formalin and stained for the assessment of fertilization. The eggs which had sperm within their perivitelline space (supplementary sperm) were defined as "penetrated" eggs. When these eggs had either enlarged sperm head(s) or male pronucleus (ei) with fertilizing sperm tail (s) in or on the vitellus, they were considered as undergoing fertilization.

Table 1 *In vitro* Fertilization of Rat Eggs

Mature female rats	Age of eggs (h after ovulation)	Sperm used	Medium used (medium : serum)	No. of females used	No. of eggs examined	No. of penetrated eggs (%)	No. of eggs undergoing fertilization (%)	No. of polyspermic eggs (%)
Naturally-ovulated	4–5	Uterine 0.5–1 h after mating	4 : 1	5	54	4 (7)	2 (4)	0
	4–5	Uterine 10–11 h after mating	4 : 0	5	56	6 (11)	4 (7)	1 (25)
			2 : 1	10	84	38 (45)	22 (26)	0
	4–5	Uterine 10–11 h after mating	4 : 1	5	55	25 (45)	25 (45)	9 (36)
	4–5 *	Uterine 10–11 h after mating	2 : 1	5	54	13 (24)	10 (19)	1 (10)
	7.5–8.5	Uterine 10–11 h after mating	2 : 1	6	78	1 (1)	1 (1)	0
	7.5–8.5	Uterine 10–11 h after mating	4 : 1	6	74	4 (5)	3 (4)	0
	4–5	Epididymal †	With serum and uterine fluid	5	52	0	0	0
Super-ovulated	1–3	Uterine 0.5–1 h after mating	4 : 1	12	280	19 (7)	4 (1)	0
	1–3	Uterine 10–11 h after mating	2 : 1	13	363	62 (17)	30 (8)	1 (3)
	1–3	Uterine 10–11 h after mating	4 : 1	4	101	22 (22)	13 (13)	1 (8)
	1–3 *	Uterine 10–11 h after mating	2 : 1	5	136	12 (9)	8 (6)	0
	1–3 *	Uterine 10–11 h after mating	4 : 1	4	133	14 (11)	8 (6)	0
	1–3	Epididymal †	With serum and uterine fluid	8	229	0	0	0

* Egg clot was washed three times before insemination.

† Epididymal sperm were incubated in the presence of uterine fluid for 2–7 h before insemination.

Fig. 1 shows a rat egg fertilized *in vitro* at the pronuclear stage. Table 1 shows that the eggs recovered from naturally-ovulated rats have a better chance ($P < 0.01$) of fertilization *in vitro* than those recovered from superovulated rats (highest penetration rates: 45% compared with 22%). The proportion of penetrated eggs was higher ($P < 0.05$) following insemination with sperm recovered from the uterus 10 to 11 h (17–45%) than 0.5 to 1 h after mating (7%) for both the naturally-ovulated and superovulated eggs. The eggs recovered 4 to 5 h after ovulation appeared to have a better chance of penetration (24–45%) than those recovered 7.5 to 8.5 h after ovulation (1–5%). By washing the egg clot before insemination, the proportion of penetration was decreased for both the naturally-ovulated (24% compared with 45%) and superovulated eggs (9–11 compared with 17–22%, not statistically significant), indicating that some beneficial factor may have been removed by washing. Although there was no obvious difference when different proportions of rat serum were added in the medium, sperm penetration was not observed when whole rat serum was used in a few experiments. Sperm penetration, however, was not observed in 52 naturally-ovulated eggs and 229 superovulated eggs when epididymal sperm, which had been pre-incubated for 2 to 7 h in the medium containing rat serum and uterine fluid, were used, they remained motile for longer than uterine-incubated sperm. This, and the higher proportion of eggs penetrated by sperm recovered from the uterus 10 to 11 h after mating demonstrated clearly that rat sperm do need capacitation in the female tract before they are capable of penetrating the egg. Hamster[6,8], mouse[15], guinea pig[17] and perhaps human[9,10] sperm can be capacitated *in vitro*, but we have shown the difficulty of capacitating rat sperm *in vitro*. Rat sperm is similar to rabbit sperm in this respect.

Of 126 eggs undergoing fertilization, 114 (90%) were monospermic and 12 (10%) were polyspermic; 12 had an enlarged sperm head and 114 had at least one male pronucleus. Fifty monospermic eggs and 12 polyspermic eggs had 1 to 26 supplementary sperm. Supplementary sperm (1 to 11) were also found in 88 unfertilized eggs, which indicates the occurrence of a vitelline block to sperm penetration as the eggs deteriorated *in vitro*. The incidence of polyspermy of rat eggs fertilized *in vivo* is about 1.2%[22]. The *in vitro* incidence of polyspermy is comparatively high as in the case of hamster[6] and mouse eggs[15]. Although fertilization of rat eggs *in vitro* was reported recently by Bregulla[20], the method used, the photographs published, and the high frequency of cleavage of unfertilized rat eggs *in vivo*[23], make his claim unconvincing.

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Receptor—Bipolar Connectivity Patterns in Fish Retina

As well as rods, there are generally three or four morphological classes of cone cells in the retinae of non-mammalian vertebrates. They are commonly distinguished as single or double cones, and they differ in other more subtle anatomical respects. Microspectrophotometric analysis of the goldfish retina[1] suggested that the red and green photopic visual pigments are located in the separate elements of the twin cones in this species, and the blue one in the single cones. More recently[2], in the frog, it has been confirmed that the different pigments are segregated into the different retinal receptor types.

We have attempted to identify the chromatic receptors of the rudd (*Scardinius erythrophthalmus*, a common European cyprinid), and to observe, from their selective neural connexions with the bipolar population, something of the way in which wavelength-specific information is conveyed between the two synaptic layers of the retina.

Besides numerous rods, the rudd retina contains the quite distinct principal and accessory elements of double cones and single cones. These three cone classes are sometimes present in nearly equal numbers, most usually in a rather disorderly mosaic arrangement. In the light-adapted retina, they are slightly displaced from one another in that order in depth, with the principal elements of the double cones furthest from the lens of the eye, and the single cones nearest to it. There is good behavioural evidence that the rudd has a photopic trichromacy like that of the goldfish[3], and it might be, as has been suggested for another species[4], that the three pigments are appropriately ordered in depth among the different cone populations to compensate for chromatic aberration in the optics of the eye. Even in the eyes of small rudd, however, the axial dispersion of red and blue light is much greater than the axial separation of the cone types. There is an additional class of tiny single cones, sparsely though regularly distributed in the retina, but their properties are beyond the scope of this account.

Lacking a microspectrophotometer, we attempted to attribute the three colour mechanisms to one or other of the three major cone types by making colour separation photographs of isolated retinae[5] that had been stripped of their rods. The tips of the cone outer segments were isolated in thin optical section, using the Leitz ×100 apochromat oil immersion objective, and recorded, by transmitted light at 430, 530 and 625 nm, on Kodak 2745 film, both before and after bleaching. The negatives were analysed for cone transmission changes at the three wavelengths with a recording microdensitometer. In good retinal preparations, the cones could be identified by their positions in depth and in the tangential receptor mosaic.

In this way, we have obtained evidence for a green-labile pigment in the accessory cones, and for a blue one in the single cones. At present it can only be argued by exclusion that the red pigment is located in the principal cones, for they have proved more difficult to register and identify, possibly because, being more distally placed in the retina, they are most likely to be distorted out of axial view. Ordering of the pigments between the cones is consistent with the sequence, if not the extent, of chromatic dispersion in the eye.

Having to that extent identified the different colour cones, we examined Golgi-impregnated retinae to establish the way in which the bipolar cells make selective contact with them in the outer plexiform layer. At the same time, it seemed important to relate such regularities as we found to other morphological distinctions between the bipolars. Although recent studies have tended to simplify this aspect of retinal anatomy, Cajal's drawings of lower vertebrate retinae[6] show rather a large number of bipolar variants in each, distinguished by, among other features, the levels to which they address their synaptic terminals among the stratified amacrine and ganglion cell arborizations of the inner plexiform layer.

Table 1 Bipolar Types Classified According to their Connectivity in the Two Plexiform Layers of the Retina

	Receptive field diameter	Inner plexiform terminal strata	Receptor input (approximate numbers refer to cone types only)	Parthe's nomenclature
A	30 μm, 0.5°	6	Rods and principal (4) cones	Small rod bipolars
B	60 μm, 1.0°	6	Rods and principal (10) cones	Large rod bipolars
C	20 μm, 0.3°	1	Rods, principal (4) and accessory (4) cones	Small cone bipolars
	20 μm, 0.3°	2	Rods, principal (4) and accessory (4) cones	
D	75 μm, 1.25°	1, 4, 6	Single (15) cones	Large cone bipolars
	90 μm, 1.5°	4,5	Accessory (25) cones	
E	40 μm, 0.6°	4,6	Rods, principal (8) and accessory (8) cones	—

Receptive field dimensions in column 1 are approximate, and converted into angular subtense on the basis of the size of the fish used. Column 2 gives the strata in which the terminal swellings are located, and the system of their numbering is shown in Fig. 1*a*. Receptor input is specified in column 3, with approximate numbers in the case of the cones, and Parthe's[7] nomenclature is given in the right hand column.

In the rudd, the inner plexiform is organized into six strata, which are often clearly visible by phase contrast in the osmium–dichromate fixed material used for Golgi-impregnation. Therefore it has been possible, in well oriented radial retinal slices, to specify the strata in which particular silvered bipolars terminate, before going on to characterize their outer plexiform connectivity. We have distinguished nine such bipolar types, and have determined the outer plexiform connectivity patterns of seven of them in the following way.

Tangential thin sections for electron microscopy were taken from the layer of rod and cone terminals at the distal margin of the outer plexiform, to locate those that were innervated by the silvered dendritic processes of particular named bipolars. The only criterion for synaptic relationship was that the processes be seen clearly to invaginate the single central cavities of the receptor terminals, and no account was taken of apposed membrane specializations or of proximity to terminal synaptic bars. The terminals of the different cones are difficult to distinguish from one another directly, but since the axons of the three major cone types preserve their

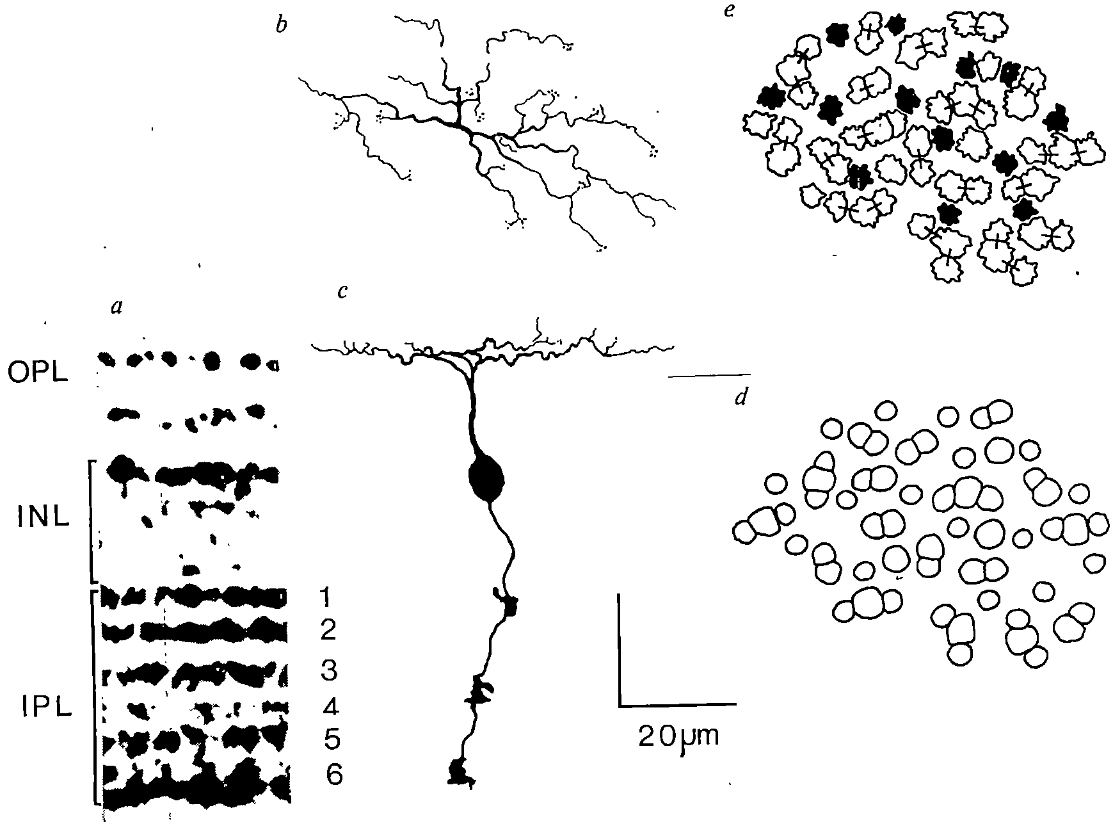

Fig. 1 The synaptic arrangements of a bipolar specific for single cones. *a*, Phase contrast micrograph of a thick radial slice of the retina to show the six strata of the inner plexiform layer (IPL) and the limits of the outer plexiform (OPL) and inner nuclear layer (INL). *b* and *c*, Camera lucida sketches, made with a × 100 objective, of the tangential and radial profiles, respectively, of the Golgi-impregnated bipolar. The terminal synaptic swellings in the inner plexiform layer (*c*) were in register with strata 1, 4 and 6. Their tangential ramifications were incompletely impregnated. *d*, Tracing from light micrographs made at the level of the cone inner segments in the retinal area overlying the bipolar cell. Single cone locations are indicated by the smaller circles, and the double cones and several anomalous single principal elements and triples by larger circles or combinations of them. *e*, Tracing from tangential plane electron micrographs of the layer of cone terminals. Terminals that received silvered synaptic processes from the bipolar dendritic tree are filled black, and can be identified as belonging to single cones by comparing their layout with *d*. The pairing relations of double and triple cone terminals are indicated by short bars. In both *d* and *e* the rare fourth cone type (see text) is omitted from the maps. The calibration bars apply to all parts of the figure.

neighbour relations as they course through the outer nuclear layer, they can confidently be identified by comparing their arrangement in the EM sections with the locations of the various cones distal to the external limiting membrane, established by sectioning at this level for light microscopy.

Fig. 1 illustrates the outcome of this procedure for a bipolar that has terminal swellings in three of the inner plexiform strata, and connects exclusively to the pedicles of single cones in the outer plexiform layer. Table 1 summarizes the principal features of the bipolar types we have studied. From their general morphology, it has been possible, with one exception, to identify them with one or other of four bipolar categories recognized by Parthe[7] in the fish retina, and we confirm the clarity of the distinctions made in that work. But for the rudd at least, some of the category names are inappropriate in the receptor connectivities they impute (Table 1), and some of them must be sub-divided to accommodate differences in the synaptic arrangements of the bipolars in the two plexiform layers.

Some functional aspects of this bipolar taxonomy deserve brief comment. First, in view of the classical distinction between the rod and cone bipolar systems[6,7], it has been surprising to find such widespread convergence of the two receptor types onto common bipolar cells. In fact, Stell[8] has shown that Cajal's[6] rod bipolars in the goldfish retina receive also cone input. In the rudd, this is true for both of the quite distinct varieties of these neurones (Table 1, *A* and *B*), and both of them draw their cone input exclusively from the principal cones, which we take to constitute the red mechanism. Further, there is rod input to those small field bipolar cells that we equate with a class previously designated exclusive to cones[7] (Table 1, *C*).

Both principal and accessory cones converge onto these small bipolars (Table 1, *C*), which are probably relatively numerous. Recordings from fish retinal ganglion cells have shown[9] that there is widespread opponent interaction between the red and green cone channels, both within spatially antagonistic receptive field regions, and between them. There is no evidence at all of additive interaction between these receptor systems, and our anatomical finding therefore suggests that the red–green opponency may arise peripherally in the opposite synaptic effects of the two cone types on the small bipolars, rather than by interaction between bipolars in the inner plexiform layer.

There is some circumstantial support for this suggestion in recent ganglion cell recordings[10,11], which have shown that, just as the principal-accessory small field bipolars receive rod input (Table 1, *C*), so the red–green opponent units are driven by the rods when they are adequately dark adapted. The sign of the response mediated by the rods (on or off-discharge) is always the same as that of the red mechanism in light adaptation, and opposite therefore to green. It is interesting that the outer plexiform connectivity of the classical rod bipolars (Table 1, *A* and *B*) is consistent with this basic synergy of the red cones and the rods. The principal cone and rod inputs to these neurones presumably operate quite separately according to the adaptational state of the retina, and it would therefore make little sense for their synaptic effects to be of opposite sign.

A final curiosity is that the bipolars that selectively innervate just one colour channel (Table 1, *D*) perform the widest spatial summation of all the types we have encountered. Their receptive fields are larger than those of the classical rod bipolars, of which one would, by tradition, expect the least acuity. Oddly enough, they are larger than the dendritic fields of at least one ganglion cell class in the inner plexiform layer.

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Phosphodiesterase in Tongue Epithelium: Activation by Bitter Taste Stimuli

THE role of cyclic nucleotides in stimulus-response coupling at the cellular level has received much attention[1]. The level of adenosine cyclic 3′,5′-monophosphate (cAMP) is dependent on its rate of synthesis, catalysed by adenyl cyclase, and on its rate of destruction, catalysed by phosphodiesterase. Although most investigators have measured the regulation of cAMP levels by alterations in adenyl cyclase activity, others have noted the presence of high levels of phosphodiesterase in certain sensory receptors and have suggested that this enzyme may be of special importance in such cells[2]. We studied the phosphodiesterase activity in tongue epithelium to determine whether unusually high levels of this enzyme might also be associated with taste receptors, and to explore the possibility that taste stimuli might affect phosphodiesterase activity, thereby altering the intracellular cAMP concentrations.

Bovine tongues were obtained at a local slaughterhouse. The dorsal epithelium of the anterior portion of the tongue was dissected away from the underlying muscle, cut into small pieces, and frozen. Frozen pieces of epithelium were homogenized in a Waring Blendor in 4 ml. of ice-cold 0.1 M phosphate buffer (*p*H 7.1) per g of tissue. Most of the insoluble material was collected by centrifugation (28,000*g* for 1 h at 3° C) and discarded. The supernatant fluid was fractionated with $(NH_4)_2SO_4$ and the fraction soluble in 20% $(NH_4)_2SO_4$, but not in 40% $(NH_4)_2SO_4$ was collected. This fraction was redissolved, dialysed against 1 mM $MnCl_2$, then centrifuged for 10 min at 20,000*g* to remove precipitated material. The supernatant solution is the "extract" referred to below; the yield is approximately 150 mg of protein for every 100 g of tissue. No phosphodiesterase activity was detected in any fraction other than that precipitating between 20 and 40% $(NH_4)_2SO_4$, nor was any activity detected before dialysis against $MnCl_2$. This procedure is identical to that used in preparing an extract which, in the presence of sweet taste stimuli, undergoes changes in its ultraviolet spectrum[3], and differs from a procedure described earlier[4,5] only by the addition of the final dialysis step. Protein content was determined by the biuret reaction[6].

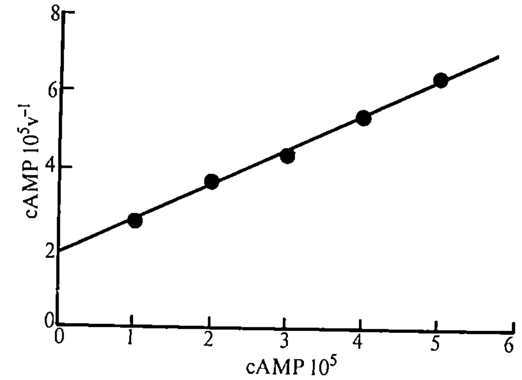

Fig. 1 Effect of substrate concentration on the hydrolysis of cAMP by the extract. Plotted according to the linear rearrangement of the Michaelis–Menten equation $S/v = S(1/V_m) + K_m/V_m$. The units of v are nmol min^{-1} mg^{-1} of protein. Assayed at 30° C by the method of Drummond and Perrott-Yee[10]. The concentrations of the components of the reaction mixture were as follows: tris(hydroxymethyl)aminomethane, 75 mM; $CaCl_2$, 1 mM; $MnCl_2$, 1 mM; 5′-nucleotidase, 6.7 µg ml.$^{-1}$ (0.08 units ml.$^{-1}$); extract protein, 0.32 mg ml.$^{-1}$; adenosine deaminase, 0.17 µg ml.$^{-1}$ (0.04 units ml.$^{-1}$); cAMP, as indicated; *p*H 7.2.

The variation in the rate of hydrolysis of cAMP with varying cAMP concentrations is shown in Fig. 1. The behaviour is consistent with simple Michaelis-Menten kinetics, with a K_m of 2.0×10^{-5} M and a V_m of 1.1 nmol of substrate hydrolysed per min for every mg of protein. The values of K_m differed very little in different preparations, while V_m varied from 0.4 to 1.5 nmol min^{-1} mg^{-1}. These kinetic parameters are within the usual range encountered in mammalian tissue extracts[7].

Preliminary experiments showed that some compounds which taste bitter resulted in increased phosphodiesterase activity when added to the extracts. Fischer and Griffin[8] have published taste thresholds for a number of compounds, all determined under the same conditions and on persons selected as sensitive tasters, and their data were used to compare the potency of the compounds as taste stimulants with the effects of the compounds on phosphodiesterase activity. Seven structurally diverse compounds with widely varying taste thresholds were selected for study. The results are shown in Fig. 2. No attempt has been made to subject the concentration dependences to a theoretical analysis. Although there is considerable scatter in the points, the concentration of each compound which results in a 25% increase in the phosphodiesterase activity can be estimated with a reasonable degree of confidence. This concentration, which is referred to for brevity as "C_{25}", is compared with taste thresholds in Fig. 3. The correlation is obvious. The straight line in Fig. 3 has a slope of 1.0, indicating that the potencies of the compounds as bitter taste stimuli are directly proportional to their potencies as activators of phosphodiesterase. The threshold concentration is usually about one-tenth the concentration which activates phosphodiesterase by 25%. The data cover a range of taste thresholds from 3×10^{-6} M to 1×10^{-1} M and suggest that the primary

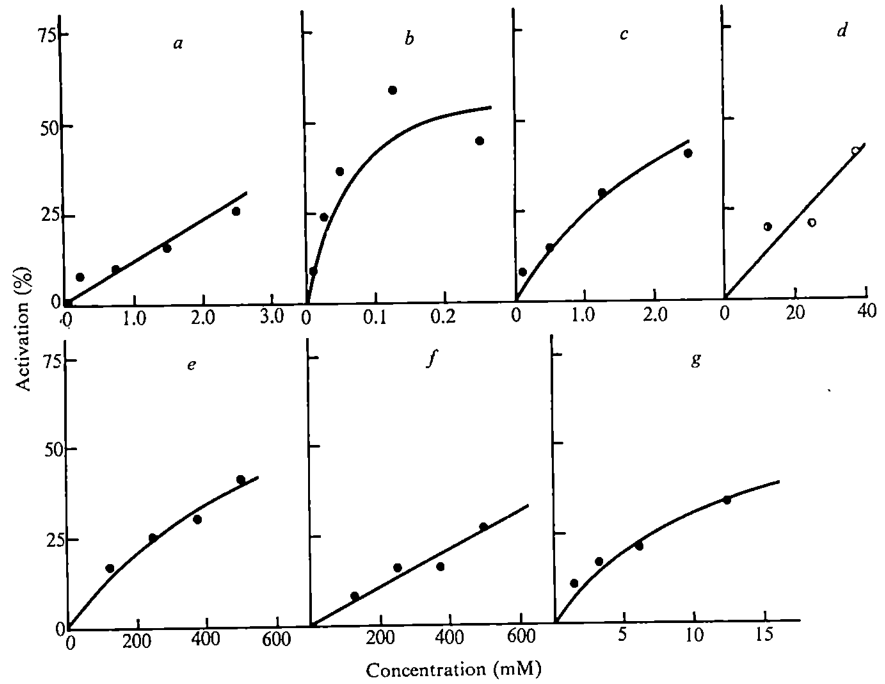

Fig. 2 Activation of phosphodiesterase by bitter compounds. Activities were measured at 30° C by the method of Butcher and Sutherland[11]. The composition of the reaction mixture was as described in Fig. 1, except that adenosine deaminase was omitted and the cAMP concentration was 1 mM. The reaction was stopped after 2 h of incubation by adding 0.5 ml. 1.2 M perchloric acid to 2.0 ml. reaction mixture, then determining P_i colorimetrically. Each point is an average of three experiments. *a*, Thioacetamide; *b*, quinine; *c*, propylthiouracil; *d*, phenylalanine; *e*, urea; *f*, acetamide; *g*, thiourea.

action of these compounds in stimulating bitter taste receptors is the activation of cyclic nucleotide phosphodiesterase. It is assumed that mammalian taste mechanisms are similar at the receptor level.

Imidazole, Mn^{2+} and Mg^{2+} are well known activators of phosphodiesterase[7], and each tastes bitter. Strychnine and nicotine, both of which are bitter[9], activate phosphodiesterase with values of C_{25} of approximately 7×10^{-5} M and 7×10^{-4} M, respectively. The only exception to the correlation of phosphodiesterase activation with bitterness which we have encountered is caffeine. Although bitter, caffeine is an inhibitor of phosphodiesterase from other tissues[7], and inhibits the activity in our tongue extracts.

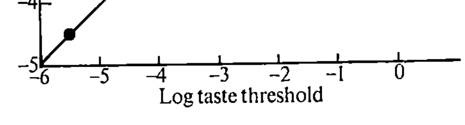

Fig. 3 The logarithms of C_{25}, determined from the data in Fig. 2, plotted against the logarithms of the taste thresholds reported by Fischer and Griffin[8].

Our data suggest that reduction of cAMP level is involved in the excitation of bitter taste receptor cells, and that activation of phosphodiesterase is among the mechanisms by which bitter compounds cause this. Thus, an enzyme which is a ubiquitous component of mammalian tissues may play an integral role in the stimulation of bitter taste receptor cells. This is consistent with the report that taste buds do not appear to contain unique proteins[12].

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Inter-hemispheric Transfer of Meaningful Visual Information in Normal Human Subjects

IN an earlier study[1], normal human subjects made fewer recognition responses to complex random shapes[2] successively exposed in opposite visual fields than to those exposed twice in the same visual field. Subjects demonstrated superior recognition of shapes exposed twice in the same visual field even though vision was allowed in one eye during initial exposure and in the other during the recognition test. As each visual field projects to the contralateral cerebral hemisphere, the results were interpreted as indicating that lateralized complex visual input does not automatically traverse the corpus callosum.

The two studies reported here were undertaken to determine whether stimulus association value affects visual recognition under conditions of successive exposure in the same or opposite visual field.

In the first experiment, 48 volunteers were randomly divided into two groups. None of the subjects wore glasses or had any other known visual defect. Sixteen trigrams were selected as stimuli; eight had an association value $\leq 25\%$ and eight had an association value $\geq 75\%$[3]. The eight high association value trigrams were: MSQ, TLW, BXT, PNK, HPD, CHF, JRN, ZBR; the eight low association value trigrams were: JBP, TZH, BFM, KXN, RGW, CSF, QWJ, FHL. The association value of these trigrams was determined by calculating the proportion of subjects in which each trigram elicited at least one meaningful associated thought or image. Each trigram was printed in black block letters 0.96 cm high on a white background and subtended 4° of visual angle. A 'Gerbrands' tachistoscope presented each trigram for 150 ms. Prior to trigram exposure, subjects focused on the point of intersection of a 2.54 cm black cross in the centre of the white pre-exposure field. The midpoints of the trigrams lay 5° to either the left or right of the pre-exposure fixation point.

The experiment was divided into initial exposure and recognition test periods. During initial exposure, twenty-four subjects were shown four low association value trigrams, two in the left visual field and two in the right visual field, each presented twice. For each subject, random procedures determined which four trigrams were to be shown and the order in which they were presented. Twelve subjects were tested with vision in their left eye blocked, twelve with vision in their right eye blocked. The other twenty-four subjects were shown four high association value trigrams under the same conditions.

Subjects were instructed to pay close attention to the trigrams because a recognition test would occur later. Approximately 2 s prior to each exposure a verbal "ready" signal was given. Subjects then fixated the point of intersection of the cross. To minimize the possibility of verbal mediation, subjects were instructed to count backwards from 100 in units of 3 as rapidly as possible for the duration of the exposure series. This technique has been successfully employed in studies of short term memory[4]. Approximately 10 s elapsed between the offset of a trigram and the onset of the next ready signal. Between 1 and 2 min after the end of the exposure series, each subject was again shown a series of trigrams and tested for recognition of those seen in the earlier series. The recognition test consisted of all eight trigrams, the four shown in the initial exposure series and four novel control trigrams, of either high or low association value. The trigrams were each exposed once, in random order, in one visual field under monocular viewing conditions. Half the subjects were tested for recognition with vision blocked in the same eye as during the exposure series and half with vision blocked in the opposite eye. Half the subjects tested with each eye had all eight trigrams exposed in the right visual field and half had the trigrams exposed in the left visual field. The experimental procedure was identical to that employed during the exposure series, with the exception that subjects were not required to count backwards. Subjects responded with a "yes" or "no" to indicate recognition or lack of it. Of the eight trigrams shown during the recognition test, two had been previously exposed in the same visual field, two had been previously exposed in the opposite visual field, and four had never before been presented.

For each subject in the low and high association value groups, the number of recognition ("yes") responses was calculated for trigrams previously exposed in the same visual field, those exposed in the opposite visual field and those never before presented (control trigrams).

These data are presented in percentage form in the upper portion of Table 1. An analysis of variance yielded the following results: (*a*) A significantly different number of recognition responses was made to the control, same field and changed field trigrams ($F=23.15$, d$f=2/92$, $P<0.01$); and (*b*) a significant interaction between association value and trigram category (control, same visual field, changed visual field) was obtained ($F=3.64$, d$f=2/92$, $P<0.05$). t-Tests performed on the interaction data yielded the following results: (*a*) For the low association value trigrams, those exposed twice in the same visual field were recognized more frequently than those exposed twice in opposite visual fields ($t=2.11$, d$f=23$, $P<0.05$), though the latter were not recognized more frequently than the control trigrams ($t=1.77$, d$f=23$, $P=$n.s.); (*b*) for the high association value trigrams, those exposed twice in the same visual field were not recognized more frequently than those exposed twice in opposite visual fields ($t=0.44$, d$f=23$, $P=$n.s.), though the latter were recognized more frequently than the control trigrams ($t=7.44$, d$f=23$, $P<0.01$).

Table 1 Percentage Recognition Responses to Control, Changed Field and Same Field Trigrams

Association value	Control	Trigrams Changed visual field	Same visual field
Experiment I (between-subject)			
Low ($N=24$)	34.37	50.00	72.91
High ($N=24$)	25.00	70.83	66.66
Experiment II (within-subject)			
Low ($N=48$)	38.02	54.17	73.96
High ($N=48$)	29.17	65.63	67.71

Contrary to expectation, stimuli exposed in the right visual field (to the left hemisphere) were recognized no more frequently than stimuli exposed in the left visual field (to the right hemisphere).

In the second experiment, another forty-eight visually normal volunteers were exposed to both high and low association value trigrams. Twenty-four subjects were first exposed to and tested on low association value trigrams and then, following a 2–3 min rest interval, exposed to and tested on high association value trigrams. The remaining twenty-four subjects received the sequence in reverse order. The procedures for selecting and presenting the trigrams during initial exposure and recognition test periods were identical with those used in the first experiment. The trigrams used in the second experiment were the same as those used in the first study. The results of the second study are presented in percentage form in the lower portion of Table 1. Analysis of variance yielded results identical with those obtained in the first experiment.

The lower portion of Table 1 shows that, while high association value changed field trigrams were recognized about as often as same field trigrams (65.63 *vs* 67.71%, respectively), low association value changed field trigrams were recognized less often than same field trigrams (54.17 *vs* 73.96%, respectively).

Collectively, the data from these two studies indicate that visual information of low association value, when projected to one cerebral hemisphere, does not readily traverse the corpus callosum. Visual information of high association value is apparently more readily transmitted between hemispheres.

Our results are in essential agreement with those reported by other investigators working with surgically prepared cats[5,6]. Chiasma-sectioned cats were first taught monocular visual discriminations of varying degrees of difficulty. Following training, either the corpus callosum was sectioned or the "trained" visual cortex was ablated, and the "untrained" hemisphere was then tested for retention of the previously learned discrimination. Retention by the untrained hemisphere was evident only for the easier discriminations.

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Long Term Effects on Immune Function of Early Nutritional Deprivation

Severe nutritional deficiency in early infancy arrests natural growth and maturation[1], resulting in depression of cell number and intellectual function of the brain in animals and man[1,2]. In experimental animals, nutritional deprivation during gestation, or lactation results in permanent reduction in mature body size and organ weight with a decrease in metabolic efficiency[3], even when optimum diets are fed after weaning. These effects are most severe when malnutrition occurs during both gestation and lactation; the most profound changes being in brain and thymus[3,4]. A similar long term effect of early nutritional deprivation on the developing immunological system has been suggested to occur in man[5].

We have examined the effect of a defined period of nutritional deprivation in infant mice at the time of weaning on the subsequent capacity of these animals to generate specific cellular and humoral immune responses to transplantation antigens. As infantile protein–calorie malnutrition in man is rarely found in the absence of infection, a further group of mice was subjected to intense antigenic stimulation during the period of nutritional deprivation. All animals were returned to a full, normal diet after a 2-week deprivation period and were tested for their capacity to develop allogenic cellular cytotoxic and haemagglutinating responses between 5 and 12 weeks later.

Male C_3H_f/Umc low pathogen mice were weaned at 20 days of age and each litter distributed at random among four dietary groups. Normal protein diets were prepared according to the formula (g dry weight per 100 g diet): casein (N : 1.5%) 30, mineral mixture USP XIV 4, vitamin mixture 2, agar 1 (Nutritional Biochemicals Corp.), dextrose 28, corn starch 28, corn oil 7. Low protein diets contained casein 6, and other components as in the full diet with corresponding increases in dextrose and corn starch. Both these diets were fed *ad libitum*, but exact quantities of each diet actually consumed were measured daily. Low-protein-low-calorie diets were prepared at twice the concentration of all ingredients in the low protein diet, with corresponding reduction of dextrose–corn starch content. Animals on this low calorie diet were fed half the dry weight per day actually consumed by low protein diet animals, thus receiving similar intakes of all components except carbohydrate. A fourth group of animals was fed the 6% casein diet *ad libitum*, and in addition received two intraperitoneal injections of 0.1 ml. killed pertussis vaccine (approximately 10^9 organisms) 1 week apart. All groups of mice were commenced on diets at 21 days of age and continued for 14 days, following which all groups received the full 28% casein diet for the duration of the experiment.

C_3H_f/Umc mice in the four early dietary groups were inoculated with 30×10^6 viable DBA/2 P-815-X2 mastocytoma ascites tumour cells by intraperitoneal injection at 10 weeks, 13 weeks and 17 weeks of age (after 5 weeks, 8 weeks and 12 weeks on the full protein diet). Spleens, lymph nodes and sera were collected 11 days later. Cytotoxic cellular immunity was measured in this allogenic system by the mastocytoma ^{51}Cr release method of Brunner[6] as modified by Canty and Wunderlich[7]. Percentage specific lysis was calculated from the formula:

Percentage specific lysis =

$$\frac{\text{c.p.m. of specimen} - \text{c.p.m. with non-immune cells} \times 100}{\text{total releasable activity} - \text{c.p.m. with non-immune cells.}}$$

Radioactivity was measured using a well-type gamma counter (Nuclear Chicago Corp.). All experiments were performed in triplicate.

Haemagglutinating antibody was determined by the PVP method[8] using allogenic erythrocytes from DBA/2 mice. Results were expressed as mean reciprocal log titres.

The cytotoxicity *in vitro* of lymphoid cells by anti-theta-C_3H antibody and rabbit complement was performed by a two-stage test described by Raff and Wortis[9]. Anti-theta-C_3H serum

Table 1 Long Term Effects of Nutritional Deprivation at Weaning on Cytotoxic Cellular Immune Responses Tested by *in vitro* Assay after 5, 8 and 12 Weeks on a Normal Diet

Diets at weaning	Total calories/mouse day	Cell-mediated lysis 5 weeks C.p.m. ± s.d.*	% Lysis†	8 weeks C.p.m. ± s.d.	% Lysis	12 weeks C.p.m. ± s.d.	% Lysis
28% Casein	8.5	4,178 ± 396	82	4,036 ± 421	78	4,294 ± 398	84
6% Casein	8.0	1,452 ± 189	18‡	2,058 ± 245	32‡	4,028 ± 476	78
6% Casein half calorie	4.0	707 ± 131	8‡	1,322 ± 141	15‡	3,057 ± 321	56‡
6% Casein pertussis	9.0	4,170 ± 449	81	3,962 ± 381	76	3,763 ± 411	72
Non-immune mice		674	0	668	0	584	0

* Mean c.p.m. and s.d. ^{51}Cr released from DBA/2 mastocytoma target cells during 2 h incubation with sensitized C_3H spleen cells at 1 : 100 ratio. Total releasable activity in each test was adjusted to 5,000 c.p.m. There were ten mice per group.

† Percentage specific lysis of target cells.

‡ Significantly different from values in normal diet mice ($P < 0.01$).

was absorbed *in vitro* with AKR thymocytes[10] and *in vivo* in theta-deprived CBA/H mice[11–12].

The mean body weights of mice fed both the low-calorie diets (64% of mean body weight of controls) and low-protein diets with antigenic stimulation (67% of controls) during the 2 weeks after weaning, remained significantly lower than control mice fed the high-protein diet when measured 8 weeks after ceasing the restricted diet.

Cytotoxic cell mediated immunity, measured by *in vitro* assay (Table 1), remained normal in animals fed 28% casein diets and also in those fed low-protein diets with antigenic stimulation. Animals fed low-protein diets at weaning showed decreased cytotoxic cellular immunity 5 weeks and 8 weeks after returning to a normal diet, but by 12 weeks these responses had returned to normal. Animals fed the more severe low-protein-low-calorie diet after weaning showed a more severe deficit of cytotoxic cell mediated immunity after 5 and 8 weeks on a normal diet and recovery was incomplete at 12 weeks.

Table 2 Long Term Effects of Nutritional Deprivation at Weaning on Haemagglutinating Antibody Titres tested 12 Days after Primary Allogenic Tumour Cell Inoculation and after 5, 8 and 12 Weeks on a Normal Diet

Diets at weaning	Mean log haemagglutination titre 5 weeks	 8 weeks	 12 weeks
28% Casein	4.3	4.5	4.4
6% Casein	3.6*	4.1	4.2
6% Casein half calorie	2.7*	3.9	3.9
6% Casein pertussis	4.8	4.9	4.7

* Significantly different from normally fed mice ($P<0.01$).

Table 3 Long Term Effects of Nutritional Depletion at Weaning on Lymphoid Cell Population in Spleen Lymph Nodes and Thymus

Diets at weaning	Weeks on normal diet	Total No. lymphoid cells spleen*	Percentage theta positive† Spleen	 Lymph nodes	 Thymus
28% Casein	5	128±8.2	36	52	79
	12	136±7.3	34	48	76
6% Casein	5	92±5.2	16‡	32‡	57‡
	12	114±6.5	32	36‡	77
6% Casein half calorie	5	76±4.1	11‡	21‡	49‡
	12	93±4.8	26‡	34‡	72
6% Casein pertussis	5	145±8.3	33	46	77
	12	163±8.7	29	49	79

* Mean ±s.d. $\times 10^6$.

† Calculated from the number of mononuclear cells per organ, the percentage lymphocytes in stained smears and the percentage reduction in mononuclear cells after treatment with anti-theta serum compared to reductions after normal AKR serum.

‡ Significantly different from normal animals ($P<0.01$).

Decreases in haemagglutinating antibody responses were significant only in the low-protein and low-protein-low-calorie groups of mice when tested after five weeks on a normal diet (Table 2).

After 5 weeks on the normal diet both low-protein and low-protein-low-calorie groups of animals had significantly reduced numbers of theta-positive lymphoid cells in spleen, lymph nodes and thymus. By 12 weeks on the normal diet both groups had more normal proportions of theta-positive cells in spleens (Table 3).

Severe protein calorie malnutrition causes extensive changes in the structure and function of the immune system in man and animals[13,14].

In this study, mice subjected to nutritional stress at the time of weaning showed persistent deficits in cytotoxic cellular immune function, reduced numbers of thymus derived (theta-positive) lymphoid cells in spleen, thymus and lymph nodes and diminished specific antibody responses.

The depression in cell mediated immunity and relative deficits of theta-positive cells in spleens and lymph nodes, were proportional to the degree of early nutritional deprivation both in extent and duration before recovery. These findings show a striking parallel with the effects of surgical removal of the thymus at a similar age[15] and suggest a maturation arrest of the thymus-dependent lymphoid system through "nutritional thymectomy" in infancy. Other factors, such as the presence of an immuno-suppressive mouse virus activated by nutritional stress cannot, however, be excluded.

Animals in this study who received intense antigenic stimulation, in addition to a restricted protein diet, showed no demonstrable deficit in immune function when tested 5 weeks later. Their mean body weights were, however, significantly lower than mice fed the low-protein diet alone.

Severe kwashiorkor commencing very early in infancy has been associated in man with profound depression of total serum immunoglobulin levels and immunological defects, components of which persisted after refeeding[16], suggesting a maturation arrest of the B cell system similar to the arrest in the T cell system suggested in this study, and by our previous observations in man[5].

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Seasonal Variations in Bone Mineral Content after the Menopause

PHOTON absorption techniques for measuring bone mineral content *in vivo*[1] have made possible realistic assessment of short-term sequential changes in skeletal mass in human subjects. Shimmins *et al.*[2], using a photon absorption technique to measure the mineral content of the third metacarpal of human volunteers claimed a reproducibility for the method of ±3% (1 s.d.). In post-menopausal women there is skeletal wasting resulting in an average fall in bone mineral content of about 1% per year[3] (post-menopausal osteoporosis[4]). Successive measurements of bone mineral content made in a group of post-menopausal women at six-monthly intervals would be expected to show a mean fall of only 0.5% on each occasion. The difference between any two such measurements should be within the reproducibility of the method, ±3%. Preliminary investigations using this method for confirming the expected reproducibility of the method gave results very much greater than ±3%, inferring that either gross technical irregularities had appeared or specific biological changes were occurring. A more detailed investigation of the problem revealed some unexpected and interesting results.

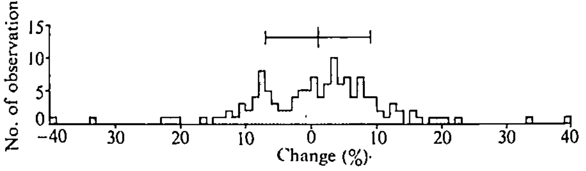

Fig. 1 Histogram showing percentage six-monthly change in metacarpal mineral content in 55 post-menopausal women.

Fifty-five post-menopausal women attending a clinic because of skeletal pain were examined. We measured metacarpal mineral content at six monthly intervals for up to two years, using a photon absorption technique[2]. The percentage difference between successive measurements was calculated, and the 130 results were plotted as a histogram (Fig. 1). The mean percentage error of ±8% was more than twice the expected error, but the distribution suggested the existence of two separate populations; one recording predominantly negative changes and the other predominantly positive changes, with the maxima at −8% and +4% respectively. Because these women were somewhat heterogeneous, and many were receiving a variety of different medicaments, we extended the investigation to a group of healthy post-menopausal women.

Table 1 Percentage Six-monthly Change in Metacarpal Mineral Content in 48 Post-menopausal Women, according to the Month in which the Last Measurement was Made

Month	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
No. of observations	8	10	16	16	11	13	8	10	16	16	11	13
Mean percentage change (±s.e.m.)	*−3.9 (±3.0)	−4.4 (±2.6)	−0.9 (±1.6)	−1.2 (±1.6)	†+2.7 (±0.8)	†+4.4 (±2.5)	*+4.8 (±1.7)	+2.7 (±3.1)	+1.3 (±2.6)	−0.7 (±1.1)	†−2.9 (±2.1)	†−4.7 (±2.4)

* $P<0.05$. † $P<0.02$.

Forty-eight healthy female volunteers aged 36–56 yr who had at some time in the previous six years undergone bilateral ovariectomy and who were thereby post-menopausal had repeated measurements of metacarpal mineral content made at six-monthly intervals for either one or two years. The percentage differences between consecutive six-monthly measurements were grouped according to the month of the year in which the latest measurement was performed (Table 1). It can be seen that there was an overall rise from January to July with the former being 3.9% lower and the latter 4.8% higher than the previous measurement ($t=2.52$, $P<0.05$). Similarly the differences between May and November were +2.7% and −2.9% respectively ($t=2.53$, $P<0.02$), and the differences between June and December were +4.4% and −4.7% respectively ($t=2.65$, $P<0.02$). Only very small differences were seen when consecutive measurements were made in March and September and April and October and vice versa. Since the number of observations in each month was small, the mean change in the whole of the winter period (November to February) was compared with the mean change for the whole of the summer period (May to August). The mean winter change (±s.e.m.) was −4.01% (±1.21), whereas the mean summer change was +3.63% (±1.10). These differences were very highly significant ($t=4.67$, $P<0.00001$). The mean differences from March and April to September and October remained insignificant.

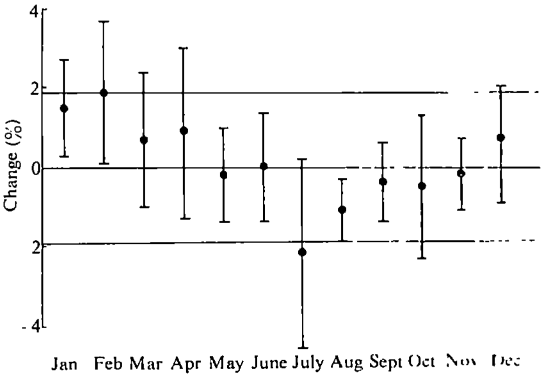

Fig. 2 Percentage change in aluminium standard according to month in which measurement performed. (0% = overall mean; means ±1 s.d. shown for both overall mean and monthly means.)

To ensure that these trends were not methodological in origin an aluminium standard, which introduced attenuation of the photon beam comparable with a human metacarpal, was scanned under the same conditions at frequent intervals throughout the second year of the study. During this period 78 standard scans were made of which 95% were within ±3.8% of the mean. The extent to which the mean of all the standard scans done in any one month deviated from the overall mean is shown in Fig. 2. The mean percentage difference found for each of the twelve months did not differ appreciably from the overall mean. Furthermore, the lowest mean standard reading was found in July, when the *in vivo* measurements were highest and the highest mean standard readings were found in January and February when the *in vivo* measurements showed some of the greatest falls. Hence the small trends which were found in the standard scans would have tended to nullify the *in vivo* changes which were actually observed and which might therefore have been even more significant, had the variations found in the standard scans not been present.

This investigation has shown that highly significant seasonal variations in bone mineral content occur, with increments from winter to summer and decrements from summer to winter; little change being seen from spring to autumn or vice versa. The increments could be explained by an increase in vitamin D activity from increased exposure to sunlight in the spring and summer. This would infer the presence of asymptomatic vitamin D deficiency. The total surface area of osteoid in the bones increases with age in women after the fourth decade of life[5], suggesting defective mineralization of osteoid as is seen in vitamin D deficiency states. Serum vitamin D activities in post-menopausal (Michigan) women are higher in the summer than the winter[6]. Also serum phosphorus[7] and calcium concentrations rise from winter to summer, and this is consistent with a humoral response to vitamin D. Whether or not such humoral changes could explain our findings must await further investigation, but the possibility that sub-clinical vitamin D deficiency might be a contributory factor in post-menopausal osteoporosis is of considerable interest.

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Tissue Zinc in Malignant Disease

It was reported by two of us that liver-zinc concentration is significantly higher in subjects dying from malignant disease than in non-malignant control series[1]. The increase was confined to parts of the liver which showed no macro or microscopic evidence of carcinomatous invasion. (The zinc content of the malignant deposits themselves is lower than that of normal liver.) Three explanations were considered. First, it was possible that the rise in liver zinc reflected a widespread premalignant change not peculiar to the liver. Second, it could be related to the poor nutritional state of most patients dying from malignant disease. Third, it could be a feature of the chemical defence reaction of normal liver tissue to invasion by malignant cells. These possibilities were further explored by measuring the zinc concentration in the liver, kidneys, heart muscle, spleen and pancreas of a further series of subjects. The analytical methods were as reported previously[1,2]. The results (Table 1) confirm the increase in liver zinc in apparently normal tissue in subjects dying from carcinoma but show no comparable increase in the zinc concentration of the kidney, heart, spleen and pancreas. The scatter of results in lung tissue was too wide to allow a firm negative conclusion.

Table 1 Tissue Zinc Levels in Subjects with and without Malignant Disease

Tissue	Malignant disease Mean	s.d.	Control series Mean	s.d.	*P*
Liver	837	204	538	95	<0.05
Kidney	502	154	505	106	>0.49
Heart	301	98	364	69	>0.25
Spleen	169	64	196	42	>0.25
Pancreas	263	104	291	126	>0.30

Zinc values in mg per 100 g ashed tissue.

The findings make it unlikely that the accumulation of zinc in the apparently healthy liver of carcinomatous subjects is a reflexion of a widespread premalignant change; and it is similarly improbable that the liver alone would be affected by the patients' poor nutritional state. We therefore conclude that liver zinc concentration rises probably as part of the normal tissue's biochemical defence reaction to invasion by malignant cells. Such an invasion in the course of a fatal malignant disease is probably invariable, the vast majority of invading cells being eliminated by the host tissue. Zinc also accumulates in granulation tissue and in and around healing wounds[3,4]; and it is conceivable that the two reactions have biochemical features in common.

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Cannabis Induced Impairment of Performance of a Divided Attention Task

An important factor in driving skill is the information processing ability of the driver. The human operator can process less information within a certain time if it must be received from more than one source[1]. Driving is such a situation and can be described as a divided attention task in which the driver is forced to perform a compensatory tracking task while searching for and recognizing environmental signals[2]. Our subjects were required to monitor and respond to two types of visual signals from different sources. We compared the effect of cannabis on the performance of subjects with and without previous experience of cannabis.

Ten male volunteer subjects had not used marihuana before the experiment and ten were experienced social users. Median use was once a week for three years but this varied within the group. The two groups were matched for age and education.

Cigarettes were prepared containing 700 mg of placebo material (extracted plant material, smelling and tasting very similar to the active material), 450 mg placebo and 250 mg active material, and 200 mg placebo and 500 mg active material. The cannabis, assayed by gas chromatography, was found to contain 1.32% Δ9-THC giving an administered dose of 3.3 mg of Δ9-THC in the low dose cigarettes and 6.6 mg at the higher dose level (Casswell and Marks, in preparation).

Using a double blind design the placebo and two dose levels of cannabis were administered in counterbalanced order on three separate testing occasions, approximately one week apart. A standard paced method of smoking was used in which each inhalation was held for 30 s. The naive subjects were all tobacco smokers and able to inhale. A highly significant ($P < 0.001$) dose-related effect of cannabis on pulse rate indicated that Δ9-THC was being absorbed by both naive and experienced subjects. The divided attention task was started 30-40 min after the subjects had finished smoking the cigarette.

The subject faced a central light surrounded by 10 peripheral lights spaced at 15° intervals on a 150° horizontal perimeter. The central light flashed at the rate of one per second with randomly programmed breaks in the flashes at the rate of one break every 20 s. The subject was required to press a key every time he detected a break in the sequence of centre light flashes. The peripheral lights were programmed to flash randomly with each light flashing 12 times during the 40 min the subject performed the task. The subject was required to press a second key in response to a peripheral light signal.

Significantly more of both central light signals and peripheral light signals were missed by the subjects after smoking cigarettes containing Δ9-THC than after smoking placebo material. Another result of major interest was the lack of significant difference between experienced and naive subjects in the amount of impairment obtained.

Table 1 Mean Number of Signals Missed following the Three Administrations for Naive and Experienced Subjects

Δ9-THC (mg)	Mean No. of misses centre light signal		Mean No. of misses peripheral light signal	
	Naive	Experienced	Naive	Experienced
0	1.6	2.4	6.1	5.0
3.3	4.3	6.2	9.0	9.1
6.6	8.1	7.4	13.7	9.3
F values	9.25		4.19	
P values	<0.001		<0.01	

The results were tested using two-way analyses of variance. F values are for drug-level effect. Between groups effects were non-significant for both central and peripheral signals.

This decrement in performance on a divided attention task is similar to that found following alcohol intoxication which is believed to be associated with the frequent occurrence of alcohol-related accidents[3].

These results, showing impairment on a dividend attention task following doses of Δ9-THC comparable to those used socially[4], support a previous finding of impairment of performance of a combined tracking and stimulus recognition task following an unknown amount of cannabis smoked in a social setting[5]. Results showing approximately equal impairment for experienced and naive subjects conflict with reports of experienced users that they do not have trouble driving when they are "high"[7]. Further, an investigation of cannabis effects on performance in a driving simulator reported no decrement in performance on several variables which have been shown to be correlated with driving performance[7]. The discrepancy between the present results and both previous laboratory results and users' reports might be explained by a difference in motivation of the subjects. The simulator task is shorter and probably more intrinsically interesting than the divided attention task used in this study. People driving after use of marihuana will of course have the threat of personal injury and expense to motivate their performance. Grinspoon[8] has suggested that motivation is an important variable in the performance of experienced users of marihuana. Motivation of subjects in a laboratory situation during cannabis intoxication must be investigated before results such as ours can be interpreted in relation to driving ability. An investigation of the motivation variable in relation to cannabis effects on performance is under way.

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A New Constituent of Biogenetic, Pharmacological and Historical Interest from *Melaleuca cajeputi* Oil

CAJEPUTI oil, obtained by the steam distillation of leaves of *Melaleuca cajeputi* Powell (Myrtaceae), has had a wide range of medical applications in the Indo–Malaysian region for many years[1]. This reputation caused it to be one of the first products brought by the Dutch to Europe from SE Asia. Several early eighteenth century publications[2] related to its introduction into Europe by the Dutch, but present day requirements are met by leaf oils of related *Eucalyptus* species. There have been, however, consistent reports regarding antiseptic and analgesic properties of cajeputi oil, which are hardly accounted for by the reported composition. This is largely cineole, together with pinene, terpineol and its simple aliphatic esters, and traces of benzaldehyde and valeraldehyde[2].

Silicic acid chromatography of a sample of the oil obtained from *M. cajeputi* trees on the campus of the University of Malaya revealed the presence of substantial quantities (about 10%) of a previously unrecorded crystalline phenolic constituent. This had the formula $C_{12}H_{16}O_4$, contained a methyl ketone system, and had mass, n.m.r., ultraviolet and infrared spectra consistent with the compound being 3,5-dimethyl-4,6-di-O-methylphloroacetophenone. This was confirmed by demethylation to 3,5-dimethylphloroacetophenone[3].

The former compound is a new natural product, and its occurrence is of interest for several reasons. First, in biogenetic terms, it is the most highly methylated simple acetogenin known, with C- or O-methylation at all probable positions. The remaining free phenolic group is strongly hydrogen-bonded, and in analagous situations (for example, the 5-hydroxyl of flavones) is rarely substituted. This emphasizes a tendency for production of highly alkylated acetate-derived polyphenols in the Myrtaceae, other examples being the chromones of *Eugenia* and *Backhousia*, phloroglucinols in *Baeckea*, and flavones in *Eucalyptus*[4].

Second, as simple phenols have antibiotic properties and these are increased markedly by alkylation of the aromatic ring[5], the occurrence of substantial quantities of this compound in cajeputi oil provides a rational explanation for the antiseptic properties. More speculatively, oxidative degradation of the compound under crude distillation conditions might well yield (as the aromatic ring is protected by complete substitution) a salicylic acid homologue with analgesic properties.

The third point is in relation to the past trade in cajeputi oil. Early European supplies were coloured green, and partly from confusion regarding the sources and production of the oil, this came to be regarded as an essential attribute. A suitable dye was often added to those batches that did not possess the "correct" colour, and eventually the green colour was linked with the use, in some localities, of copper distillation vessels for production of the oil. This is hardly a complete explanation, however, as the recorded constituents should have no interaction with copper, and the effect has been attributed to such causes as traces of butyric acid released from the terpinyl ester, itself a minor constituent. The β-hydroxyketo grouping present in 3,5-dimethyl-4,6-di-O-methylphloroacetophenone is an extremely effective chelating system for metals, and the ease with which it forms a soluble complex with copper provides the other half of the answer to an early mystery of the spice trade.

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Evidence for Apostatic Selection by Predators using Olfactory Cues

MANY visual predators hunt in a frequency-dependent manner, and can actively maintain colour polymorphisms in their prey[1–3]. These predators tend to concentrate on common varieties of prey, and to overlook rarer forms even if they are obvious. This type of behaviour is responsible for apostatic selection[3], and has been interpreted as being due to the formation of "specific searching images"[4–6].

We have tried to discover whether predators behave in a similar manner when they are using olfactory, rather than visual, cues. As predators we used an outbred laboratory stock (Edinburgh Q) of *Mus musculus* L. The "prey" were artificial baits, cylindrical in shape (6 mm in length, 3 mm in diameter) made of five parts by weight plain flour and four parts lard. They were scented with peppermint essence (J. M. Bannerman and Co. Edinburgh: 2.5 ml. to 40 g dough) or vanilla (Crosse and Blackwell Ltd London: 5 ml. to 40 g). Edible brown dye (Scottish Flavour and Colour Co. Ltd Edinburgh) was added to give them identical value ("lightness") and chroma (strength of colour) and nearly-identical hue on the Munsell Scale[7]. The colour-scores were 2.5 Y 4/8 for peppermint-flavoured baits and 2.5 YR 4/8 for vanilla. A slight difference in hue, just visible to the human eye, was due to colouring already present in the vanilla essence.

The predators were conditioned by exposing them to twenty baits of one variety for a period of ten minutes on three consecutive days. Variation between individuals was reduced by hand-feeding each mouse when necessary to ensure that it had eaten a total of twenty baits during the conditioning period. Tests were carried out on the fourth day, offering the predators equal numbers of the two types (ten of each) set out in an alternating rectangular array. Conditioning and testing were conducted in the same area against a background of stiff white paper (2.5 R9N[7]) replaced after each test, and under standard illumination (an 80 W fluorescent lamp situated five feet vertically above the area). The test area was $17'' \times 14''$. The analysis was based on the first ten baits attacked by each individual during the test period. All attacks (contacts between the bait and the mouth of the predator) were counted, including those in which the baits were not eaten. To the human eye the peppermint baits (P) seemed to be more conspicuous. The vanilla baits (V) appeared to be more palatable to the mice. The probabilities quoted in the text are derived from contingency tables using the numbers of mice showing particular preferences, not the numbers of baits attacked. This avoids the possible pitfalls of assuming that each attack is an independent event.

In the first experiment, thirty naïve adult female mice were allowed their normal diet of rat cake (Edinburgh University Diet) while being trained and tested on the different odours. The results (Table 1*a*) show that mice trained on P baits attacked significantly more P than V ($P<0.02$) and that those trained on V attacked significantly more V than P ($P<0.001$). The difference in the behaviour of the two groups is highly significant ($P<0.001$).

Because the response of a predator to a particular prey can be altered by changes in the relative palatability of alternative food[8], the first experiment was repeated, under identical conditions except that rat cake was replaced by sunflower seeds, which are taken more readily by *Mus*. This might be expected to reduce the effectiveness of conditioning. Although the conditioning did indeed appear to be less effective (Table 1*b*), the results of the second experiment are not significantly different from those of the first.

Six mice that had been trained on P and six that had been trained on V were retested five days later, having meanwhile been fed on rat cake. The results (Table 1*c*) show that each group maintained its preference even after contact with the alternative bait. The difference between the two groups remains highly significant ($P<0.005$).

Eighteen mice from the original groups were retrained for three days on alternative baits to those on which they had been trained. The results given in Table 1*d* suggest that retraining has destroyed the earlier preferences. Neither group shows a significant departure from random predation, nor is there any difference between them.

Among visual predators, there is evidence that when a particular prey is at high density and there is a lack of alternative prey, "satiety" may develop[5], manifesting itself as a decreased tendency to take prey that has previously been common. An experiment was carried out to test whether this effect occurs among olfactory predators. Eighteen mice were divided into two groups, each of which was offered an excess of one type of bait for three days without alternative food. They were then tested in the same manner as before. The results (Table 1*e*) show that each group developed a preference for the unfamiliar baits ($P<0.001$). Trials with further groups of mice showed that a single day of training with excess P induced a preference for V, although the preference became more pronounced with further training. On the other hand,

Table 1 Predation by Mice of Artificial Baits Scented with Peppermint (P) or Vanilla (V)

	P trained Baits attacked by individual mice	Total	Previous total by same mice	V trained Baits attacked by individual mice	Total	Previous total by same mice
a	P 2 7 7 6 5 7 5 6 7 5 6 6 7 5 7	88	—	1 2 4 2 2 4 3 3 4 5 0 0 2 2 1	35	—
	V 3 3 3 4 5 3 5 4 3 5 4 4 3 5 3	57	—	4 8 6 5 8 6 7 7 6 5 4 6 8 8 9	97	—
b	P 1 4 5 5 5 4	24	—	3 4 3 3 1 5	19	—
	V 0 6 5 5 5 6	27	—	7 6 7 7 9 5	41	—
c	P 7 5 6 5 7 7	37	37	1 1 1 0 4 2	9	13
	V 3 5 3 5 3 3	22	23	9 9 6 9 6 8	47	44
d	P 6 4 4 4 4 5 5 5 3	40	20	4 4 6 5 5 4 5 5 6	44	54
	V 4 6 6 6 3 5 5 5 5	45	62	6 6 4 5 5 6 5 5 3	45	39
e	P 1 0 0 3 0 1 1 0 1	7	—	7 4 2 0 6 2 0 1 2	24	—
	V 9 2 3 7 6 8 2 1 9	47	—	3 3 1 0 0 1 2 1 1	12	—

a, One set of mice had been conditioned ('trained') by exposure to P baits, the other set by exposure to V baits. The alternative food was rat cake. *b*, Experiment identical to (*a*) except that the alternative food was sunflower seeds. *c*, Mice from experiment (*a*) were retested after an interval of five days. *d*, Results of 'retraining'. Mice from experiment (*a*) that have been trained on V were retrained on P, and *vice-versa*. *e*, Training by exposure to an excess of one type of prey. Note reversal of preferences compared to experiment (*a*).

a single day of training with excess V induced a preference for V, two days' training led to no preference, and three or more days' training induced a preference for P. Thus it seems that the same bait in different circumstances can be treated as palatable or unpalatable (cf. Young[9,10]).

We have found some evidence that mice can discriminate visually by tone (value[7]) rather than colour (hue[7]). Experiments using baits made distasteful with quinine suggested that the mice could discriminate between baits differing by 5 units of value on the Munsell Scale[11]. It therefore might be argued that the results of our conditioning experiments were due to visual rather than olfactory factors. This argument can be discounted, for several reasons: (i) The P and V baits differed only very slightly in hue, and not at all in value. There is no clear evidence of colour discrimination in mice[12]. (ii) Experiments in which mice were conditioned to unflavoured baits differing in value (5 units on the Munsell Scale) gave no evidence that visual preferences were developed[11]. (iii) We trained one set of three mice on dark V, and another on light P. The dark and light baits differed by five units of value. The mice were then tested on dark P and light V. The results (Table 2) show that olfactory preferences dominate any possible visual ones. The differences are significant ($P<0.05$, one-tailed) and entirely compatible with the earlier experiments.

A small additional series of experiments, similar to those already described but using long-tailed field mice (*Apodemus sylvaticus* (L.)) captured from wild populations, suggested that these predators can also develop olfactory preferences[11]. There is evidence that deer-mice (*Peromyscus* spp.) behave in a similar manner[13].

We conclude that predators hunting by smell can develop preferences for familiar types of prey. Among visual predators this kind of behaviour is capable of maintaining colour polymorphisms within the prey species[1-3]. It follows that there should be scent polymorphisms within species attacked by olfactory predators. To our knowledge, however, the only known cases of animal scent polymorphisms are Müller's[14] report of dimorphism in male butterflies (*Battus polydamus*) and some associations with mimicry[15]. Their apparent rarity may be due only to the difficulty of detecting them. Our experiments lead us to believe that this rarity is indeed more apparent than real. They also suggest that it would be profitable to search for the development of preferences among predators using other senses (the use of auditory cues by nocturnal predators, or pressure and electric fields by aquatic predators). We would expect to find corresponding polymorphisms (in sound, movement or electrical properties) among their prey.

Table 2 Tests for Visual Preferences

i, Trained on 'light' P		Total	*ii*, Trained on 'dark' V	Total
No. of dark P attacked	6 2 6	14	3 2 3	8
No. of light V attacked	4 2 4	10	7 8 7	22

Mice were trained on 'light' P and 'dark' V, but tested on 'dark' P and 'light' V. 'Dark' and 'light' baits differed by 5 units of value on the Munsell Scale[7].

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Control of Aggression by Singing in Crickets

ETHOLOGISTS developed the idea that many animal species evolved mechanisms to control aggression among their members. This control is by the use of signals to reduce the probability of attacks by the opponent before injurious or lethal combats occur[1–3]. Although there are observations that are best explained by the theory, no direct experimental evidence has been presented. We report here one type of experimental evidence that seems to fit the theory.

Cricket fights have been a popular sport in China since ancient times[4]. When two adult male crickets are put together in an empty aquarium containing just one burrow for hiding, they fight over it. The winner and the loser are determined during the initial phase through vigorous battles. After this period, actual physical combats occur less frequently because the subordinate cricket tends to avoid encounters with the dominant one either by not approaching it or by getting away from it.

Acoustic signals seem to play an important role in the proceeding and outcome of an encounter. Adult male crickets produce several types of sound. A male, perched alone at the entrance of his burrow, gives the calling song, the most commonly known chirping of crickets. When two male crickets come close or engage in a battle, they raise their wings and produce the so called aggressive or rivalry song. Dominant males sing more aggressive songs than subordinate males and the amount of aggressive stridulation is positively correlated with winning encounters[5].

We have found that deafening an adult male cricket immediately makes it more aggressive. Crickets of the species *Acheta domesticus* and *Gryllus pennsilvanicus* were deafened by tearing the tympana in the forelegs under ether anaesthesia. This operation abolished the responses of the tympanic nerve to a play-back of recorded chirps as monitored electrophysiologically. The sub-genual organ in the foreleg and the cerci responded to low frequency tones. These organs perhaps cannot register the stridulatory sounds, the frequency range of which lies between 3 kHz and 6 kHz in *A. domesticus* and 3.5 kHz and 5 kHz in *G. pennsilvanicus*. The subgenual organs in the middle pair of legs responded to recorded chirps played back at supernormal intensity. Control experiments showed that ether had no effect on the aggressiveness of the cricket.

Individuals were marked with various combinations of dots of silver enamel. In the first series of experiments, two unacquainted crickets were put together in a small cage which made frequent encounters inevitable. In this situation the crickets fought or demonstrated the dominance relationship clearly. We observed each pair of crickets until a statistically sufficient number of encounters was recorded. As Alexander[5] noted, the results of most encounters between male crickets are clear cut. In this report, we include only those encounters in which one cricket dominated the other as evidenced by the retreat or evasive behaviour of the subordinate individual after physical combats. The loser was then deafened and rematched with the winner. One example of *G. pennsilvanicus* is presented (Table 1). The deafened cricket which had lost the majority of encounters now clearly dominated its former superior rival. In all cases, the deafened losers immediately became extremely aggressive; they initiated combats and engaged in sustained battles.

In the second series of experiments three or four crickets were kept together in an empty aquarium where they freely encountered and could establish a dominance hierarchy. Again two crickets were transferred at a time to the small test cage for a bout of encounters. Each insect met every other in a tournament. This procedure enabled us to determine quickly the rank of each insect in the hierarchy. The lowest ranking insect was then deafened and rematched with all the higher ranking individuals. One example of *A. domesticus* is presented in Table 1.

Table 1 Effects of Deafening on Fighting

Crickets	*G. pennsilvanicus* Before	After	Fisher exact probability test
1→2	30	4	
2*→1	2	25	$P<0.00001$
	A. domesticus Before	After	
2→4	10	2	
4*→2	2	11	$P=0.00008$
3→4	13	2	
4*→3	1	6	$P=0.00023$
2→3	2	2	
3→2	17	11	$P=0.371$

Figures under "before" and "after" indicate the numbers of winning encounters before and after deafening. $x \to y$ indicates x won over y. The Fisher exact probability test was used to obtain the significance level of the differences in the number of winning encounters between the matches before and after deafening. Before deafening *A. domesticus* had established a dominance hierarchy in which 3 dominates 2 dominates 4. This was reversed after the deafening of cricket 4.

* Deafened cricket.

This group contained four insects numbered 1, 2, 3 and 4, which had established the following dominance hierarchy $3>1>2>4$, where $x>y$ indicates x dominates y. After the deafening of the lowest ranking cricket 4, a new rank order $4>3>(1)>2$ resulted. Since cricket 1 died before the completion of the tests, its rank was uncertain. The deafened cricket 4 dominated significantly larger numbers of encounters in the rematches with crickets 2 and 3. In the contest between the intact crickets 2 and 3, no significant change occurred between the initial match and the rematch.

In another group of four *A. domesticus* the deafened lowest ranking cricket climbed but one place in the hierarchical ladder. It could not dominate the remaining two rivals. The results of the tournament show, however, that in every rematch, the deaf cricket significantly increased the proportion of winning encounters. Alexander[5] reports that the dominance-subordinate relationship between two males could be reversed by forcing the dominant cricket to lose fights against a dummy while broadcasting synthetic or natural rivalry songs. This observation not only lacks statistical validation but also does not isolate the role of the acoustic signal, since the abortive physical engagement (antennal lashing) with the dummy alone may account for the reversal of the rank order.

We offer the following hypothesis to explain our results. The acoustic signals of the dominant cricket inhibit the aggressive tendency of the subordinate one. The inability to hear the signals of the opponent frees the deaf cricket from the inhibition. The consequence is less inhibited aggression. The incomplete reversal of rank mentioned above seems to indicate the existence of some other factors which influence the probability to win an encounter. The calling song of a male cricket not only attracts females[6] but also perhaps "warns" other males at a distance. The rivalry song which is used at a close range perhaps plays a more important role in the control of aggression.

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Population Control in Snails by Natural Inhibitors

In many areas of the world diseases such as schistosomiasis caused by trematodes, still cause misery to millions of people and much damage to livestock. Because a specific mollusc, often a snail, is necessary for the completion of the trematode life cycle, the elimination of that host would eradicate the disease. According to Southgate[1] none of the molluscicides currently available is ideal. Among their disadvantages are toxicity to organisms such as fish and the relatively high concentrations required for their effect. Here we describe a naturally occurring population inhibitor from snail cultures which because of its specificity and potency suggests another approach to mollusc control. The data presented below indicate that such substance is produced in cultures of at least two species of snails. Discovery of this inhibitor came about through an investigation into the chemical and physiological basis for the inhibition of population growth which occurs in crowded snail cultures.

Rose[2] reviewed the literature describing population restriction by crowding and indicated that it is common in plants and animals. Among molluscs, Chernin and Michelson[3,4] reported that a snail host of schistosomiasis, *Biomphalaria glabrata*, exhibited decreased growth and reproductivity when maintained under crowded conditions in the laboratory. Berrie[5] corroborated that study with observations of natural populations of *Biomphalaria* in Uganda. We studied the phenomenon in *Fossaria cubensis*, a snail vector of fascioliasis with some observations on *B. glabrata*. The *Fossaria cubensis* used in these studies were descendants of individuals collected in Angelton, Texas, where they are natural hosts to *Fasciola hepatica*. The snails were routinely maintained according to the methods of Isseroff and Read[6] except that "Cerophyll" was used as food in place of hay infusion.

Each snail was maintained separately in 100 ml. of water in a 12.5 cm vessel. Each experimental or control group contained five to ten such snail samples. Unless otherwise noted, water was changed daily in all experiments; for controls distilled water containing a suspension of non-toxic chalk (as a calcium source) was used. In the experimental group water was replaced with fresh aliquots containing the same type of chalk but with the addition of the test factor(s). Temperature was maintained at 22° C.

To isolate the active substance, water from *Fossaria* cultures at least one month old, was evaporated at room temperature to about 1/100 of its original volume in large, shallow pans. The concentrated solution was dialysed against tap water and finally against distilled water, and the dialysed concentrate saturated with ammonium sulphate to precipitate the inhibitory substance. The precipitate was redissolved in a small volume of water and redialysed to remove the ammonium sulphate which can be toxic to the snails. Generally 1 ml. of the concentrated and purified inhibitory substance(s) (IS) was added back to 99 ml. of fresh water for assay purposes. On the basis of assays, dilutions for experimental purposes were adjusted according to a standard unitage defined as the volume of the concentrate required to just produce complete inhibition of growth of a 5.0 mg snail in 4 days. Fig. 1 shows the effect of the IS isolated with ammonium sulphate at unit concentration on *Fossaria* of two different ages. Growth is inhibited within 24 h after addition of the IS. A dose-response curve for IS shows its effect is non-linear with increasing concentration and has a maximum effect at about one unit of activity (Fig. 2). The IS effect was reversible. Growth resumed after exchange of IS water for fresh water on day 4, at a rate similar to that of untreated snails in the earlier part of the experiment. IS also affects egg laying by mature snails and this effect can also be reversed when the snails are placed in fresh water (Fig. 3). Eggs normally hatch in 9–10 days. In the presence of the IS development is normal till just before hatching, when the embryos die. It has, however, little or no effect on the growth of mature snails. An interesting cross species effect of the *Fossaria* IS on egg production of *Biomphalaria glabrata* was found; over a two week period egg laying of the schistosome carrying snail was inhibited by 56%. Specificity of the IS to molluscs is suggested by studies with planaria (*Dugesia tigrina*) and platyfish (*Xiphophorus*). At concentrations ten times those effective for *Fossaria* the IS showed no effect on growth of these organisms.

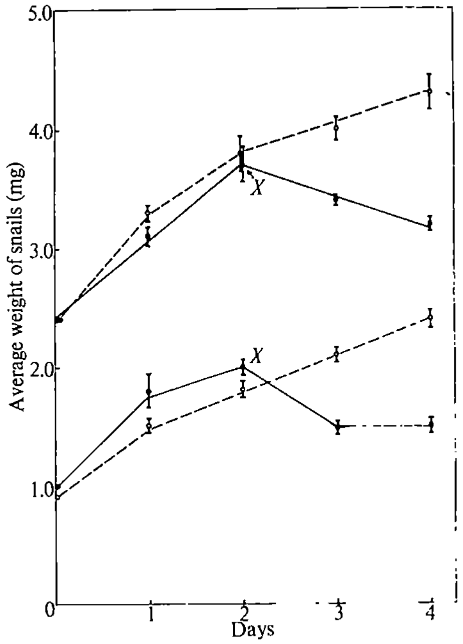

Fig. 1 Effects of unit concentration inhibitor on growth of *F. cubensis* in two age groups. Snails were permitted to grow for 2 days and IS was added after the second day to both groups (point ×). The untreated controls (○) continued to grow but growth inhibition and weight loss occurred within 24 h of addition of the inhibitor (●).

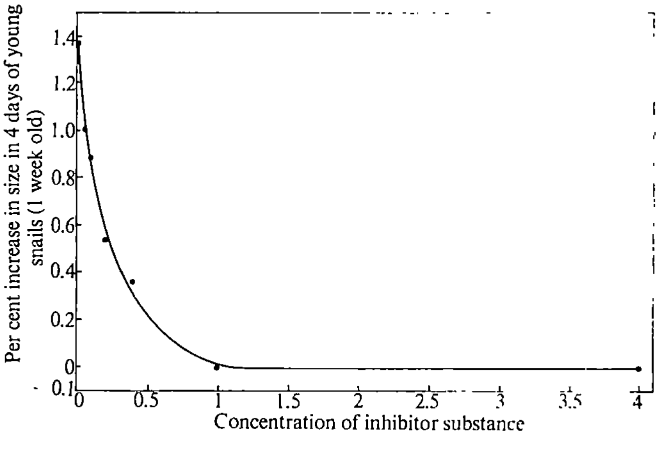

Fig. 2 Effect of increasing concentration of inhibitor on the growth of young *Fossaria*.

IS is stable for at least a month at 22° C in static, non-aerated, non-filtered tanks. At 5° C in concentrations of 1 to 1,000 it is stable for over 7 months, and is not affected by freezing, thawing, or lyphilization. Activity of the IS is completely destroyed by heating in solution at 85° C or by incubation with 1.0 ug of trypsin/ml. of diluted IS at room temperature (Fig. 4).

Our observations indicate that a chemical substance, presumably produced by *Fossaria cubensis*, can inhibit its own species growth and egg deposition. Although much work remains to be done with regard to completely isolating and purifying the IS, its physical and chemical properties indicate that it is probably a protein. Rose and Rose[7] found that the growth inhibitor released by frog tadpoles is also proteinaceous. It would be interesting to determine whether the tadpole inhibitor and snail inhibitor produce their effect by a common mechanism.

The apparent absence of an effect on snail embryos until they are almost ready to hatch may possibly be explained by supposing that the gelatinous covering of the egg mass is impermeable to large molecules such as the IS until just before hatching when the covering breaks down.

It is likely that the production of IS under natural conditions may serve to restrict population increase during the dry season when food may not be abundant. The long stability of IS in solution at room temperature also supports this hypothesis.

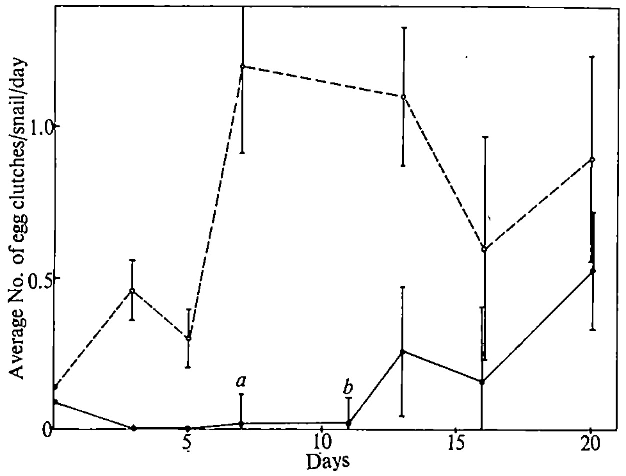

Fig. 3 Effect of unit concentration inhibitor on egg deposition in *Fossaria* (●). Egg laying (*b*) resumes when snails are placed in fresh water. (*a*) Upper curve (○) shows egg deposition during same period in fresh water.

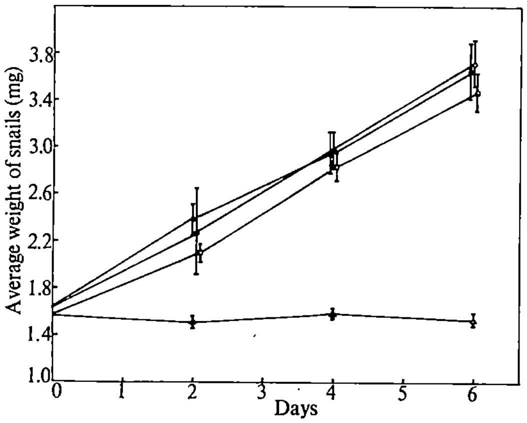

Fig. 4 Effect of adding trypsin (1 µg/ml.) to cultures of *Fossaria*. Controls containing fresh water only (☐) or fresh water plus trypsin (○), were not statistically different in growth rate from snails grown with inhibitor (unit concentration) and trypsin (●). However, growth in the presence of inhibitor (unit concentration) without trypsin (△) was almost completely inhibited.

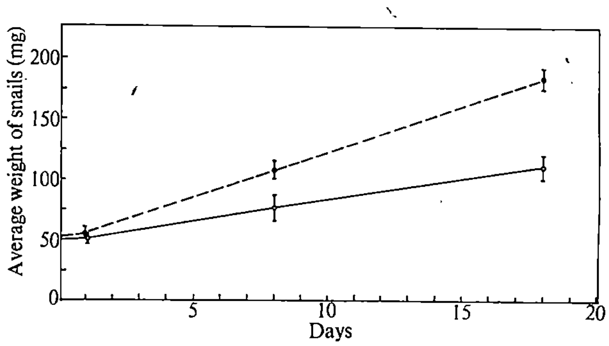

Fig. 5 Effect of unit concentration *Biomphalaria* IS on the growth of young *Biomphalaria*.

An ammonium sulphate precipitate prepared from old cultures of *Biomphalaria glabrata* has also been found to have an inhibitory effect on young *B. glabrata* (Fig. 5) and on egg production by the adults (Table 1). Experiments with *Biomphalaria* were carried out by methods similar to those used with *Fossaria*.

Table 1 Effect of Old Water from *Biomphalaria* Cultures, after Dialysis and Redilution to its Original Concentration, on Egg Laying in *Biomphalaria*

	Average No. of egg clutches/snail/day	Inhibition	Significance
Controls	15.2 ± 2.84	—	—
Experimental with old water	8.6 ± 1.12	43%	$P < 0.05$

Data taken from a 16 day experiment. Five snails in each group.

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Observation of the Pleurotomarid *Entemnotrochus adansoniana* in its Natural Habitat

THE pleurotomarids or slit-shells are the most primitive of existing gastropods and of unique malacological and conchological interest. They retain, in a particularly deep mantle cavity, what was probably the original molluscan organization of paired gills and associated organs[1]. Externally they are large top shells but with a narrow slit running far back from the outer lip of the shell. The Pleurotomariacea were originally known only as fossils, appearing in the late Upper Cambrian and attaining the height of their development during the Palaeozoic[2].

It was therefore with an excitement similar to that which later greeted the discovery of the first living monoplacophoran, *Neopilina galatheae*[3], that in 1856 P. Fischer and

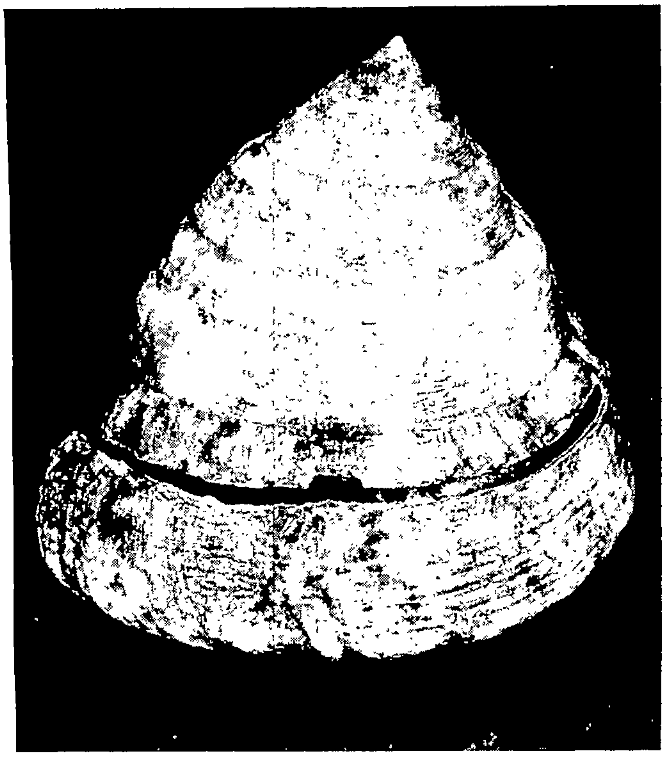

Fig. 1. *Entemnotrochus adansoniana* Crosse and Fischer, showing full extent of slit.

A. Bernardi described an empty slit-shell as *Pleurotomaria* (*Perotrochus*) *quoyana*. This had been found the previous year by Commandant Beau who collected in the Lesser Antilles and had taken it from a deeply laid fish trap into which it had been carried by its temporary occupant, a hermit crab.

This information is provided by Dance[4] who adds, that, after passing through various hands, this famous shell became part of the Mrs de Burgh collection which was acquired by the British Museum (Natural History) in 1941. It is 4.52 cm in diameter and 3.42 cm high. More specimens have subsequently been taken off Barbados, Yucatan, and elsewhere in the Caribbean and the Gulf of Mexico. Descriptions of the shell features and the anatomy of this species were later given by Dall[5] and Bouvier and Fischer[6] respectively. A fuller account of the anatomy of the Japanese species *P. Beyrichii* was provided by Woodward[7].

Fifteen species of *Pleurotomaria* divided into three sections on the basis of radular characters, *Entemnotrochus*, *Perotrochus* and *Mikadotrochus*[8], are now known, seven from the West Indies[9], the remainder from the Pacific, off Japan and round the Moluccas. All live in relatively deep water.

The first shell of *Entemnotrochus adansoniana* Crosse and Fischer, 1861, was, in the words of Dance[4], "discovered in the collection of a Dr Commarmand, unlabelled and partially broken, and it was twenty years before complete specimens were found, in the Caribbean, by the US Coast Survey steamer Blake". This second Atlantic species is some three times larger than *P. quoyana*, the dimensions of a specimen now in my possession being 14.1 cm in diameter and 13 cm high, the slit being 16 cm long (Fig. 1). Among slit-shells, this species is only exceeded in size by the Pacific *E. rumphii*.

The specimen illustrated in *Rare Shells*[4] has an interesting history, being one of a pair originating at Tobago and purchased at Barbados by an enthusiastic Victorian collector, Samuel Archer, an army surgeon from Liverpool[10]. One of the shells is now at the Liverpool, and the other at the Manchester Museum. Occasional specimens of this species have been taken during the past century, usually in depths of around 100 fathom, from the Caribbean south to Brazil.

It can now be stated to occur, and undoubtedly in some numbers, at depths of around 400 foot downwards, on the sediment covered talus slopes off the seaward face of the coral reefs along the north coast of Jamaica. These observations were made from a two-man 'Nekton' submersible operating from the Discovery Bay Laboratory[11] during August 1972.

Following intensive study over many years by the late Professor T. F. Goreau and colleagues[12,13], the reefs in this vicinity are the best known in the Caribbean, and probably in the world. Shallow water and scuba diving studies have revealed a series of zones. Inshore areas involving a shallow lagoon and a reef crest are followed by an extensive fore-reef, in exposed areas involving buttresses, and characterized by massively branching *Acropora palmata* with often hemispherical colonies of such corals as *Monastrea annularis, Millepora alcicornis, Porites astreoidea* and *Diploria strigosa* and below this an area of delicately branching, frequently broken, *Acropora cervicornis*. These occupy a gently shelving fore-reef which is succeeded by a steep fore-reef slope largely covered with sandy deposits with small species of the green calcareous weed, *Halimeda*. This comes to an abrupt end at around 150 foot where it gives place, at the "drop-off", to a vertical, in places actually overhanging, wall occasionally interrupted by shutes down which sediments periodically cascade. At the base of this wall, around 400 foot, the talus slope begins. This descends at an angle of about 45° into deep water, and appears to consist of fallen blocks and fragments covered with a thin layer of soft sediment.

The highly manoeuvrable 'Nekton' submersible (General Oceanographics, Inc.) proved an ideal vehicle for making biological and sedimentological observations from the lower level of Scuba to a depth of some 1,000 foot. The bottom could be viewed in close detail through the numerous well placed port holes in and around the nose (where the observer lies) and around the conning tower in which the pilot sits.

Epifaunal molluscs are singularly few in these environments but a large top-shell was seen on my first dive. Dr Willard Hartman reported seeing another in which he perceived indications of a slit and later a dead shell of *E. adansoniana* was secured by means of the submersible's "claw". On my last dive (piloted by Dr Land) a fine specimen was closely observed at a depth of 525 foot. It was alongside a projecting sheet-like expanse of grey sponge. The foot was partly expanded and the slit clearly lined with tissue but the epipodium with its tentacles was withdrawn. Although the entire surface of these upper talus slopes was covered with a silvery coloured layer of sediment, this was very thin and the animal must normally crawl on the hard surface immediately beneath this and is probably just as much restricted to a hard substrate as are the shallow-water Trochacea. Later information from Discovery Bay is of specimens seen on the rocky surface of the wall, as high as 380 foot, as well as one on the talus slope at 1,000 foot. Movement must be very slow because any significant disturbance of sediment would foul the deep mantle cavity with its elaborate equipment of two aspidobranch ctenidia (that is, four rows of filaments compared with the single row in the pectinibranch ctenidium of mesogastropods and neogastropods). All aspidobranch gastropods are endangered by water borne sediment[1].

The nutrition of so large an animal raises problems. The population of the escarpment above consists largely of sponges (including numerous colonies of Sclerospongiae[14]) feeding on fine phytoplankton and of gorgonids living on zooplankton. The only other conspicuous animals there and on the talus slopes are crinoids, ciliary feeders which may be collecting plankton mixed with fine organic debris. There is none of the algal life on which archaeogastropods, from *Haliotis* to docoglossid limpets and trochids, characteristically feed by means of the broad rhipidiglossan radula.

As with other groups, including ascidians and bivalve molluscs, descent into deep water has involved at any rate a partial change to a carnivorous diet in the pleurotomarids. Woodward found clear evidence that *P. Beyrichii* feeds on sponges and this is highly probable for *E. adansoniana*. However, there is the problem of the rhipidoglossate radula, here of unique width with 69 teeth on either side of the central tooth in *E. adansoniana*[5], 109 in *P. quoyana*[6] and 111 in *P. Beyrichii*[7]. These are of various merging types only two of which appear capable of tearing sponge tissue[7]; the function of the remainder remains obscure.

There is a possibility that these may be concerned with collection of fragments of weed, especially *Halimeda*, falling from above. The large *H. copiosa* Goreau and Graham is common between 30 and 240 foot especially on steep slopes[15] and was observed in abundance round the top of the escarpment. The surrounding area was covered with whitened accumulations of the characteristic segments of dead fronds. These must continuously rain down on the upper regions of the talus slope where *E. adansoniana* lives and may retain significant amounts of edible matter. This upper talus slope could well represent a unique environment particularly rich in constantly renewed supplies of organic debris.

However, there is now a possibility of resolving this and other problems concerning the life of these slit-shells, notably the functioning of the pallial and reproductive organs with information about development.

I was also able to examine specimens of *Basilomya goreaui* nov.gen.nov.sp. recently described by Bayer[16], obtained by Dr J. B. C. Jackson (Johns Hopkins University). This small dimyid bivalve, which lives on the under surface of the extensive and very thin sheets of *Agaricia* which occur around the lowest level of coral growth, was first collected by Professor Goreau in 1964. This appears to be the first time any dimyid has been examined in life.

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Specificity and Inhibition of Attraction of Male *Rhyacionia frustrana* and *R. rigidana* to their Female Sex Pheromone

Rhyacionia spp. moths (Lepidoptera : Olethreutidae) are common pests of young pines in the Southeastern United States. Although the Nantucket pine tip moth, *R. frustrana* (Comstock) is usually the most prevalent species, it is often associated with the pitch pine tip moth, *R. rigidana* (Fernald)[1,2]. No previous studies have provided information on mechanisms which isolate these two species.

Table 1 Average Number of Male *Rhyacionia* spp. Moths Caught per Trap by Live *R. rigidana* Females, Crude Tip Extracts of *R. frustrana* and *R. rigidana* Females, and Combined Extracts*

	R. frustrana extract	*R. rigidana* extract	*R. rigidana* females	Combined extracts	Control
Date		Male *R. frustrana*			
March 27	28	0†	0	NT	0
28	15	NT	0	0	0
29‡	0	0	0	0	0
30	23	0	0	0	0.3
April 1	NT	NT	0	0	0
2	8	NT	0	1	0
Total	74	0	0	1	0.3
Date		Male *R. rigidana*			
March 27	0	59†	9	0	0
28	0	NT	57	0	0
29‡	0	0	0	0	0
30	0	30	39	0	0
April 1	NT	NT	10	0	0
2	0	NT	0	0	0
Total	0	89	115	0	0

NT, not tested.

* Each figure represents the average of one to three traps with 5 female equivalents of one species, combined 5 female equivalents of both species, or five live females per trap.

† Fourteen female equivalents.

‡ Temperature ranged from 10° C to 4.5° C. No flight activity of moths was observed.

During the 1972 spring emergence of *Rhyacionia* spp. moths, a study began in Clarke County, Georgia, to determine the role of sex pheromones in separating the two species. Approximately 2,000 infested shoots of loblolly pine, *Pinus taeda L.*, were collected from two plantations and placed in a continuously illuminated screen cage (1.2 × 2.5 × 2 m) indoors. Moths were removed from the cage as they emerged and held in glass vials. The moths were separated by species using characters as previously described[1]. Females were held in the vials for one day and then the apical two or three abdominal segments were clipped off and placed in hexane-ether (1 : 1).

When moths began to emerge in large numbers in the field in late March, traps were baited at dusk on several dates with five equivalents of tip extract of female *R. frustrana*, *R. rigidana*, or a combination of both extracts, or with five live female *R. rigidana*. No traps were baited with live *R. frustrana* because it had already been demonstrated that males are readily attracted to caged females[3,4]. The trap design was the same as that described before[5]. Live females were placed in a cage in the trap and crude tip extracts were pipetted onto filter paper and placed in the trap. Unbaited controls contained filter paper only. The traps were placed in a single row about 2 m high in infested pines which averaged 2.5 m. All traps were oriented in the same direction and were spaced about 5 m apart. Traps were systematically placed so that no two identical treatments were adjacent.

The catches of male moths per trap are shown in Table 1. Crude extracts of *R. rigidana* females attracted only *R. rigidana* males and compared favourably with live females with an average of 4.9 males/female equivalent/day and 3.6 males/live female/day respectively. We have previously shown a similar relationship in *R. frustrana* emerging in the spring[4]. In the present study, crude *R. frustrana* extracts caught an average of 3.06 *R. frustrana* males/female equivalent/day.

On the basis of moths emerging in the indoor cage, *R. rigidana* made up about 10% of each of the two field populations. However, more *R. rigidana* males were trapped than *R. frustrana* indicating a stronger response to the pheromone by the males or more pheromone per *R. rigidana* female.

Traps baited with a mixture of five female equivalents each of *R. frustrana* and *R. rigidana* extracts on five occasions caught only one *R. frustrana* male but on the same nights *R. frustrana* and *R. rigidana* extracts in separate traps caught an average of 15.3 and 35.3 males of their own species per trap respectively. No cross attraction occurred with females of either species; therefore, it seems that the pheromones are different and effectively aid in isolating the two species.

Table 2 Attraction of *Rhyacionia frustrana* Males to Different Quantities of Female Tip Extracts

No. of males trapped		
1 FE	2 FE	5 FE
1±1	5±1	15±9

Each figure (±1 s.d.) is the average number of males attracted to traps containing 1, 2, or 5 female equivalents (FE) per trap in each of eleven replications with one trap per replication.

In other lepidopteran species, inhibition of male attraction has been demonstrated with live females[5] and with synthetic compounds[6–10]. In one interesting case with synthetic compounds[11] evidence was presented that the sex pheromone of one species of Gelichiid moth consisted of the *cis* isomer while that of a second species consisted of the *trans* isomer of the same compound. Mixtures (10 µg each) of the two isomers inhibited attraction of males of both species. Attraction or inhibition of attraction was not compared with live females or extracts of females; therefore, it is not known whether the sex pheromones of these two species are multi-component.

Wright's suggestion that an insect attractant may be composed of more than one chemical[12] has been supported recently with several species of moths. In most of the cases in which this point has been carefully examined, two or more components of the natural sex pheromone have been demonstrated or indicated[7,13–18]. Our data indicate that there are two or more components of the sex pheromone system of *R. frustrana.* Field tests of gas-liquid chromatography (GLC) fractions of crude extract have shown that at least two fractions were attractive alone and more attractive when combined. Also, combined GLC fractions were considerably less attractive than crude extract. According to comparisons with GLC peaks containing attractant activity, the crude extracts of female tips (five female equivalents) which completely inhibited attraction of *R. rigidana* males, contained a maximum of about 20 ng of any one attractive component.

The amount of extract from *R. frustrana* females which completely inhibited attraction of *R. rigidana* males (five female equivalents) was quite close to the attraction threshold for *R. frustrana* males (approximately one female equivalent, Table 2). These data clearly emphasize the potent inhibitory properties of these extracts.

This report is the first demonstration of complete inhibition of male attraction with extracts of females containing the full complement[4] of the natural sex pheromone system. In addition to the previously demonstrated opposite isomer type of inhibition of attraction[11], a different system of inhibition may be operating in cases involving multi-component sex pheromones.

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Chromosome Aberration Dosimetry in a Case of Over-exposure to Radiation

ESTIMATION of radiation dose to the body from the yield of dicentric chromosome aberrations in peripheral blood lymphocytes has been developed into a valuable technique in radiological protection practice[1]. It has been used as a means of resolving disagreements arising from anomalous film badge readings, and in cases of possible over-exposure where no dosimeter was worn. Another use is in the accurate estimation of dose which is necessary for determining the future employment status of exposed radiation workers, and also for guiding clinicians in the treatment of radiation injuries.

In January 1970 a radiation worker was referred to hospital with lesions on both hands; he had been working for three years with iridium-192 sources which were being used for industrial radiography purposes. Radiation injury was diagnosed. Nevertheless he continued in radiographic work until December 1971 when he was admitted to hospital where the index finger of the right hand was amputated. No satisfactory prior dosimetric data were available and it was decided to use the chromosome aberration technique in order to make an assessment of accumulated radiation dose.

From a blood sample lymphocyte cultures were made and five hundred metaphase spreads were examined with the following results: dicentrics, 49; centric rings, 7; acentric rings, 10; interstitial deletions, 31; terminal deletions, 21. Eighteen dicentric chromosomes were also found minus their associated deletions. A detailed account of the genesis and significance of dicentric and other chromosome aberrations is given by Evans[2] and UNSCEAR[3].

As about five years elapsed between the first exposure and the chromosome analysis it is necessary to take into account the rate of loss of lymphocytes from the body. By studying the fall of aberration yield with time after treatment in a group of radiotherapy patients, Norman *et al.*[4] estimated the half-life of lymphocytes carrying dicentric aberrations to be approximately 530 days. Buckton *et al.*[5] estimated 1,600 days with 95% confidence limits of 900 to 6,700 days. Our own findings of 30 months (in preparation) falls between these two estimates By taking a round figure of 1,000 days as the half-life of the lymphocytes containing dicentric aberrations, and by assuming that the radiation was received uniformly in equal annual doses during the five years, it is possible to predict that 90 dicentrics would have been found in 500 cells if no cell losses had occurred.

By reference to a calibration curve produced *in vitro* (in preparation) using cobalt-60 gamma radiation at a chronic dose rate of 18 rad $^{-1}$, this dicentric yield corresponds to an equivalent whole body exposure of 200 rad. As the person probably received the radiation dose in small increments at high dose rates spread out over five years, this might not be the appropriate calibration curve to use but we have not yet investigated the effects of dose fractionation.

We also observed in the 500 cells 18 dicentrics lacking their associated fragments. However, because the calibration curves are based solely on dicentric yield in complete cells[6] it is not possible to interpret them in terms of dose. The absence of the associated deletions suggests that mitosis may have occurred *in vivo* following irradiation. Such divisions are normally rare, but when they occur the fragments, which lack a centromere, pass wholly into one or other daughter cell. Bearing in mind that the average lifetime of mature lymphocytes may be several years, Bender[7] states that the presence of cells lacking expected fragments may indicate that the chromosome damage has been sustained over a considerable period. This theory is in agreement with the present findings where the history of malpractice is known to span five years.

Studies of this nature, especially where there is a lack of reliable physical dosimetry data, illustrate the valuable contribution which chromosome analysis is making to good radiological protection practice. In addition, the accumulation of this type of data is necessary for the eventual evaluation of risk of the late effects of radiation in terms of acute biological effect.

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Neuromuscular Control of Trumpeters' Lips

SCIENTIFIC experiments on musical performance are surprisingly sparse when one considers that neuromuscular control of skilful motor performance reaches its acme in music. A case in point is the embouchure of brass instrumentalists, that is, the control of the firmness and vibration of the lips in relationship to each other and to the mouthpiece. The pedagogical literature is in a "state of chaos" according to Weast[1]. Among anatomists little more is known today about the normal function and kinesiology of the muscles of facial expression than has been known for a century—knowledge gained through the dissection of corpses and simple observation[2]. With the exception of buccinator muscle during normal function[3,4] and labial muscles during speech[5,6], the facial muscles have been almost ignored by electromyographers. Thus, electromyography (EMG) offers to reveal the function of the facial muscles as it has for many other parts of the body[7].

With both science and art as our motives, we studied the effects of register, intensity and subjects' proficiency on the electromyographic potentials of selected facial muscles during trumpet performance by eighteen players with a wide range of experience. We recorded from bipolar fine-wire electrodes[7] in the orbicularis oris muscle in both the upper and lower lips, levator anguli oris and depressor anguli oris. Our eighteen volunteer trumpet players possess a wide range of proficiency; at the top are three concert artists and at the bottom, three high school students with limited experience. The subjects were rank-ordered according to numbers of years of private study, years played and age. All subjects were exposed to the same controlled environment, technique, instrumentation and procedures. After a set warm-up period, each subject played on cue a series of fifty-one test items for recording; these were chosen to demand a wide variety of trumpet techniques, including extremes of dynamic and pitch range. EMG activity was quantified using a four-integer system as follows: 0, nil; 1, slight; 2, moderate; and 3, marked (maximum). When testing for differences between related scores, that is, when comparing two measures on the same subject, we used the Wilcoxon matched-pairs signed-ranks test. For comparisons between independent scores, that is, measurements made on two different groups of subjects, we used the Mann–Whitney U test, as recommended by Siegel[8].

Both register and intensity positively affect the embouchure's muscle activity ($P < 0.005$), register having a greater effect than intensity ($P < 0.005$).

Advanced trumpeters have more activity in the muscles surrounding the lips than those in the lips ($P = 0.025$) in contrast to the reverse finding with less advanced trumpeters who show no difference. This negates the widely accepted "drawstring or tug-of-war" theory which proposes that the lip muscles are pitted against the other facial muscles in the correct embouchure formation. The beginners demonstrate more muscle activity in the upper lip than in the lower lip ($P < 0.005$). Although the lip muscles can be considered anatomically as a single unit (a sphincter muscle surrounding the oral orifice), functionally the lips must be considered as two separate muscles. While the data do not show that advanced trumpeters have less muscle activity in the upper lip than in the lower lip, advanced trumpeters do show a smaller ratio of upper lip to lower lip activity than beginners. This finding suggests that beginners should either concentrate more activity in the lower lip or less activity in the upper lip, or both; but the present data do not disclose which of these possibilities caused the difference between groups.

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BOOK REVIEWS

Transparent Things

Foundations of Cyclopean Perception. By Bela Julesz. Pp. xiv+406. (University of Chicago: Chicago and London, 1971.) £9.

Foundations of Cyclopean Perception is an exciting, stimulating book about one of the most interesting recent developments in perceptual psychology. It is also beautifully produced, worth buying as an object in its own right. As a book it can be read and understood on several levels. It is a mixture of transparent clarity—most of the experiments the author discusses can be attempted by the reader—and of abstraction which can be difficult and even ambiguous.

Julesz has worked on binocular interactions in human vision for about 15 years. His fundamental technique is to use a pair of patterns which give a depth percept when fused binocularly, as in a stereoscope, but which contain no monocularly perceivable form. The advent of large digital computers made the generation of such stimuli possible: perhaps Julesz's greatest achievement is his combination of modern technology with conceptually simple experiments. A typical stimulus is a pair of patterns of equal numbers of black-and-white square picture elements arranged at random in 100 element square arrays, giving the impression of randomized chess boards. Both patterns of a pair are identical except that, say, a central square portion of the array in one is shifted horizontally by an integral number of picture elements with respect to the same region of the other. When the two patterns are fused binocularly the lateral disparity leads to the percept of a central square region standing out in depth from the remainder of the fused array, which forms a rectangular surround in a different depth. Although the disparities cannot be detected by visual inspection of the separate patterns of each pair, the retinal disparities between the fused images are perceived. In normal vision such differences in retinal disparity between regions of fused images automatically lead to the perception of depth, but before Julesz's work it was assumed that the disparity information could not be used without prior recognition of forms in the visual stimulus. A clear conclusion from this kind of experiment is that depth perception, and the underlying processes required to detect the disparities between two retinal images, can be entirely central processes not requiring monocularly recognizable structure and independent of eye movements and vergence. Not only is it possible to draw conclusions about depth perception, but it is also possible to use Julesz's technique to distinguish the central and peripheral components of a wide range of visual phenomena. Many such experiments are described in the book, and the significance of their results to visual pattern processing and to general theories of neuronal function is discussed in detail.

Julesz's technique has led to two kinds of achievement; a much better understanding of the mechanisms of binocular vision and depth perception, and a method for locating function within the central nervous system. I shall not list his major results, but I do think that it is worth stressing their relevance to the most difficult unsolved problems of perceptual psychology. First, he shows clearly that "familiarity deprivation" can lead to novel and surprising insight. New kinds of stimulation may be necessary for new discoveries. Second, as had been well understood by many earlier workers, the use of binocular interaction is an extraordinarily powerful tool for locating visual function. Obviously it provides a way of separating peripheral from central components of a percept, but more than this, a hierarchy can be built up, in which the relative level of a function can be assigned a place. For example, in some circumstances it is clear that motion perception can occur after fusion, at a higher level than the pattern-matching process for random dot stereograms. In this case the stereograms were used to separate cues for movement that are inextricably mixed in normal vision.

There are several irritating aspects to the book—for example, considerable redundancy—but as a whole it is a huge achievement, making an original synthesis of visual perception and providing stimulation and suggestions for experiment that will be hard to exhaust. I think that some of the material is included prematurely, for example, sections on eidetric imagery and model building, but for many readers these may well provide a feeling of more immediate contact with work actually in progress.

In short, Julesz has written an original, idiosyncratic, immensely exciting and beautiful book. It deserves a wide audience, particularly because almost all the experiments described can be performed by the reader using the anaglyph representations of Julesz patterns (which, incidentally, are of the highest quality that I have seen printed). The accessibility of the results makes it much easier to accept Julesz's slightly dogmatic style, and gives one a much greater feeling for the synthesis of perceptual psychology and neurophysiology towards which Julesz is continually pointing, and without which an understanding of perception is impossible.

ANTHONY ROBERTSON

Wallace and Darwin

Wallace and Natural Selection. By Lewis McKinney. Pp. xix+193. (Yale University: New Haven and London, September 1972.) $12.50; £4.95.

DR MCKINNEY has given more than six years of close study to Alfred Russel Wallace. He has traced minutely the intellectual and empirical sources of that great naturalist's thoughts on selection, and has carefully documented the relations between Wallace and Darwin. The results appear in this book—an elegant and readable piece of scholarship, drawing together a vast quantity of published and archival material. The microscopic examinations of Wallace's deception over the actual place of his "sudden insight" into the mechanism of evolution, and the even more interesting deception by Darwin over Wallace's 1858 paper, are fine examples of historical detection. Some intriguing questions emerge, and we can perhaps expect McKinney to pursue these in future writings.

On broad historiographical grounds, however, there are two grave defects in this book. The first is McKinney's unconsidered approach to the way religion and science interacted in the nineteenth century. He cites the historian Hooykass ("religion→science") favourably, but elsewhere couches his descriptions of Wallace in terms that overstress his own ahistorical biases: Wallace was "essentially unprejudiced by religious preconceptions"; "unencumbered by religious ties", and so on. This language is too value-laden.

Secondly, McKinney seems to be wholly unaware of the social and political contexts of evolutionary biology. Some of the very material he cites patently indicates Wallace's early meritocratic view—a view which needed the philosophical (and psychological) support provided by natural selection theory. McKinney does not catch this.

Nor does he seem to know of recent work by R. M. Young and others on the specific ideological backgrounds of Chambers, Malthus, Darwin and Wallace himself. Natural selection was such a useful political tool, and arose at such an opportune time, that it is hard to believe its originators were unmotivated by "external" (that is, non-scientific) factors. The single external factor in McKinney's book (aside from religion, which he mishandles) is Wallace's ambition. Otherwise, McKinney concentrates only on intellectual motives, and though he does this very well, the resulting explanation is insufficient for modern history.

It is as if by reading *Vestiges,* Lyell and Malthus, spurning religion and dabbling in natural history (which is all Wallace did at first), anyone could have hit on a mechanism of evolution, perhaps natural selection itself. Yet hundreds of intelligent men did just these things (in spite of McKinney's denial — unfootnoted — of widespread atheism) without such results. So what really did happen that led Wallace to this grand theory?

As yet, Dr McKinney has provided only a fraction of the answer. Because he is such a fine scholar, however, we must hope that he can widen his view.

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Atmosphere of Stars

Basic Physics of Stellar Atmospheres. By T. L. Swihart. Pp. viii+86. (Pachart: Tucson, 1972.) $7.95.

THIS is a short text covering the theory of stellar atmospheres for the non-specialist. It consists of four chapters covering the equation of transfer and formal solutions thereof, the grey atmosphere, model atmospheres and line formation. An appendix summarizes physical and astronomical constants and presents a number of exercises.

The book seems inferior to other recently offered stellar atmosphere texts. The aspects of the field treated in any detail exclude any of the important recent developments. For example, while the Avrett-Krook temperature correction procedure is derived in some detail there is nowhere mentioned the linearization methods developed by Auer and Mihalas which will soon displace the above procedure in essentially all aspects of model building.

The author explains in the preface that his approach is basically physical as opposed to mathematical. By this he apparently means that he includes specifically the microscopic physics that go into the radiation transfer process. In so far as he carries that philosophy the derivations and discussions of the input physics are very clear and readable. Yet I am amazed at the almost complete absence of a discussion of continuous absorption processes. A novice reading this as an introduction to the field would be left with the impression that essentially the only relevant source of continuous opacity is that of the H^- ion. The possibility of neutral hydrogen as a source of opacity is mentioned in only two sentences in the entire book. The neutral hydrogen absorption cross-section is never presented and the idea of opacity discontinuities is completely missing. This is somewhat surprising in that perhaps the most important aspect of model stellar atmospheres is their ability to predict the continuous spectra of stars and how they depend on temperature and gravity.

The lack of discussion of the macroscopic aspects of the physics of stellar atmospheres is also disturbing. Very few concrete results are given. What are typical densities in the photospheres of B stars and of M stars? What are the electron donors across the H-R diagram? Where is H^- important? Neutral hydrogen opacity? Molecular opacity? In short we find the discussions to be rather sterile and far more mathematically oriented than implied in the author's preface.

The execution of this book also leaves something to be desired. Different faced typing is often slightly displaced below the rest of the text which is disconcerting. The only two illustrations are interchanged. The rather thick covers contribute almost half of the total thickness of the book.

This book is the first of a series of "Intermediate Short Texts in Astrophysics" to be published by the author and his colleague, A. G. Pacholczyk. As with any "first", there are many lessons that can be learned here.

D. M. PETERSON

Mycology from India

Hyphomycetes: An Account of Indian Species, except Cercosporae. By G. V. Subramanian. Pp. xi+930. (Indian Council of Agricultural Research: New Delhi, 1971.) Rs.50.

PROFESSOR G. V. SUBRAMANIAN is an acknowledged expert on the Hyphomycetes and a book by him dealing with this difficult group is to be welcomed. On opening the book it is, however, something of a disappointment to find that, although the publication date is 1971, the monograph was prepared in 1961 and contains no references to publications later than 1962. In view of the attention given to this group in the last decade by mycologists all over the world, including the outstanding contributions made by Professor Subramanian himself and his students, it is to be hoped that the publishers will give him the opportunity of bringing it up to date in the near future.

The first part (some 180 pages) gives an informative account of the early work on Hyphomycetes, of their general structure, habitats and importance in industry and agriculture, and discusses heterocaryosis, classification and nomenclature. In view of the author's own critical studies the section on classification is of particular value. A clear account is given of attempts up to 1961 to formulate a more natural arrangement than Saccardo's system which, while useful as a means of identification, brings together obviously unlike organisms in the same genera. Professor Subramanian adopts a system based on those of Hughes and Tubaki but gives his own definition of spore types. Since during the last decade there have been a number of other discussions and criticisms of the Hughes/Tubaki suggestions it is particularly unfortunate that this book does not contain Professor Subramanian's own more recent modifications of the system he proposed in 1961. It does, however, offer a firm basis for appreciation of recent contributions. This general section concludes with a useful bibliography of work published before 1962.

The greater part (Part II) of the book is devoted to descriptions of all species of Hyphomycetes recorded in India up to 1961/2, amounting to over 500 species. Necessary additions to and revisions of this part to bring it up to date are likely to be relatively unimportant. Part II begins with a useful key to genera and at appropriate places in the text keys are given to Indian species of each genus. Full and clear descriptions of all genera and species are given, together with brief notes on habitat and distribution. Most species are illustrated by clear line diagrams.

This book represents years of painstaking and accurate work on this difficult group of fungi. In spite of the delay in its publication, it is a substantial and welcome addition to the literature and will prove to be invaluable, not only to Indian mycologists, but to all students of the Hyphomycetes and to plant pathologists.

The book is worthy of stronger binding (which does not stand up to normal handling of a volume of more than 900 pages) and of better quality paper. It is to be hoped that its success will warrant an early revision giving full justice to the author's scholarship and critical powers. L. E. HAWKER

Membranes and Ions

Biophysics and Physiology of Excitable Membranes. Edited by William J. Adelman, jun. Pp. xiv+527. (Van Nostrand Reinhold: New York and London, January 1972.) £12.25.

Membranes. Edited by George Eisenman. Vol. 1. *Macroscopic Systems and Models.* Pp. xix+333. (Marcel Dekker: New York, May 1972.) $19.50.

IT is curious that at a time when research on cell membranes has become such a fashionable field, there should be so few textbooks dealing adequately with certain aspects of the subject. The appearance of a book from which, to quote its dust cover, one "can gain a broad view of the theoretical approaches and technical procedures now used in excitable membrane biophysics" is therefore welcome. But as is too often the case with multi-author texts, the quality of the articles is variable and there are some surprising gaps in their coverage. Thus as far as voltage clamp studies are concerned, it seems a pity that a critical and helpful account of the application of the technique to myelinated fibres should be accompanied by one on giant axons that is marred by its cursory dismissal of the problems arising from the potential drop across the series resistance R_s due to the presence of the Schwann cell. As K. S. Cole points out in his historical survey, Hodgkin and Huxley took some pains to compensate electronically for at least part of R_s, but many of their successors have simply ignored the series resistance. In a fresh axon the resulting current-voltage curves may be displaced by many millivolts from their correct position. The subject is not well served by glancing over this admittedly technically troublesome point when at the same time considerable space is devoted to the questionable advantages of voltage-clamping with continuously varying command potentials instead of discrete steps.

It is surely odd that a chapter entitled "The Thermodynamic Foundations of Membrane Physiology" should make no mention at all of experimental investigations on the calorimetry of the nerve impulse. And although the mechanism of active transport of ions in nerve and muscle is dealt with very adequately, almost nothing is said about the measurement of the downhill ionic movements during nervous activity. There are useful chapters on other topics such as the X-ray analysis of myelin structure, optical studies, perfusion of giant axons, drug action, and experiments on model membranes. But the claim of the book to conduct a thorough "in-depth" examination does not seem entirely justified.

A similar claim is made for the volume edited by Professor Eisenman, this time more justifiably since it is the first of a series of unspecified length. Volume 1 sets the stage, containing accounts of the physical chemistry and theoretical background for the penetration of ions across different types of membrane, such as those with neutral pores, ion-exchange resin membranes, liquid membranes and dry silicate membranes. Volume 2 will be wholly concerned with the ionic conductance of artificial lipid bilayers incorporating carrier-type and tunnel-forming ionophores. This seems a logical scheme, and the last two chapters in Volume 1 are therefore a little out of place, consisting as they do of some purely theoretical arguments about excitable membranes, and of a mainly technical account of a new method for turning squid axons inside-out. In spite of the ingenuity of this procedure it is not clear that it has any marked advantage over existing perfusion techniques.

R. D. KEYNES

Human Error

Human Factors in Highway Traffic Safety Research. Edited by T. W. Forbes. Pp. xix+419. (Wiley: New York and London, June 1972.) £7.85.

SCIENTIFIC investigations towards an understanding of driving behaviour and a theory of accident causation have been conducted in such diverse fields as highway and traffic engineering, ergonomics, psychology, and driver education. Perhaps because of this, such research is not always accessible to the engineers who are charged with the task of designing a safe transport system for human use. Human factors is one of the newer engineering disciplines which attempts to assess the design implications of behavioural studies.

This book, which has contributions from seventeen authors, specialists in a particular area of human factors studies, summarizes research on the biographical and physiological characteristics of drivers, factors in sign legibility, other methods of presenting information to drivers, skills, judgment and information acquisition in controlling vehicles in traffic, impairment of driver performance due to such factors as fatigue, alcohol and drugs, the effect of psycho-social factors such as stress, driver education and improvement. It can be seen from the comprehensive range of topics covered that of necessity it can only serve as an introduction. Each section is extensively referenced, however, thereby making a very valuable contribution. Consequently this may be of interest to students on courses of highway and traffic engineering as well as practitioners in the field of road safety. The extent to which it can be effective in arousing students' interest in the implications of their work as engineers, as an isolated course, is unknown.

The main area of concern, however, is the extent to which an approach such as this can achieve the stated objective of designing the man–machine environment task and/or system to fit human capabilities wherever possible. In principle this seems to be a very interesting approach. But most of the analysis is conducted in a vacuum quite distinct from actual accident occurrence. No attempts were made to show how this type of formal model, especially with regard to car following, overtaking, and so on, had any predictive validity. Indeed, the author concluded that drivers do a remarkably good job even in a system where breakdown appears to be inevitable. Perhaps this very observation suggests that the system analysis approach is not valid.

The cybernetic models proposed in most chapters to describe the driver–car–road environment system equated man with a limited capacity information-processing channel and driving as a negative feedback control system. It seems unlikely that a theory of driving which makes such simplistic assumptions about the driver will be very useful. Such a theory denies the possibility that he may initiate any action. Driving is only one of a range of social activities which is influenced by the behaviour of other people and as such is affected by the prevailing social mores which may be antipathetic to safety. While this book gives a good coverage of topics related to human factors, contributions from social psychologists are omitted.

Given this uncertainty about the validity of the model, the ability of this type of approach to help the engineer design a system to cater for human capabilities may, therefore, be very limited. JEAN SHAOUL

Biological Electron Spin

Biological Applications of Electron Spin Resonance. Edited by Harold M. Swartz, James R. Bolton and Donald C. Borg. Pp. x+569. (Wiley Interscience: New York and London, September 1972.) £11.55.

ELECTRON spin resonance spectroscopy was discovered in 1945, and first applied to biology in 1954. In 1958 Ingram produced the first book on applications of e.s.r. outside physics, and included a short chapter on biological and medical applications. The length of the present book shows that the subject is still growing according to an exponential law. How much has been accomplished in the 18 years since the first publication?

A quick glance through this book shows that e.s.r. is now being applied throughout biology, at the molecular level. It is particularly valuable in the study of photosynthesis; of enzymic reactions, especially those concerned with electron transport; of radiation biology and of various aspects of cancer. In the spin label method, which first appeared in 1965, there is a technique whose possibilities seem to be limited only by the ingenuity of the investigator. On the technical side of e.s.r. there have been great advances. Spectrometers are now reliable and easy to use, and the recent coupling of spectrometers to computers has led to improved spectra and improved analysis of spectra. The present book contains a detailed and valuable chapter on quantitative e.s.r. However, the basic problem remains, that on the one hand cells are complex and on the other hand e.s.r. spectra obtained from them are, in most cases, relatively nonspecific. So the use of e.s.r. has not led to any major advances in biology; nevertheless all biologists who are interested in the molecular aspects of their subject should be aware of the potentialities of the method.

How suitable is the present book as an introduction to e.s.r. for biologists and physicians? The editors, two physicians and a chemist, produced it because of their belief that the full potential of e.s.r. in biology was not being realized, principally because biologists did not have an adequate understanding of this method, and that a principal obstacle was the lack of a good text directed towards biologists. Accordingly the book begins with an explanation of the method, on a three-level approach, excessively simple in the introduction, and as simple as possible in the first three chapters, with more advanced material set off in small type. Although all biologists and physicians will be able to follow the introduction. I am less sure about the explanatory chapters, where one is rapidly plunged into the mysteries of tensors, axes of symmetry, slow exchange and fast exchange, crystal field splitting etc. Most biologists and physicians, I feel, will heave a sigh of relief when they reach the more familiar ground of "Cells and Tissues" in chapter 4. My advice to them would be to skip the early chapters, to go straight to the applications, which are covered very thoroughly, and then, if they want to use e.s.r., to get the collaboration of a physicist or chemist who understands the technique.

The book is written by ten authors, and suffers inevitably from some lack of cohesion and some variability of standard. However, the treatment never drops below an adequate standard, and I recommend it as essential reading for all biologists approaching e.s.r. for the first time, and an essential acquisition for libraries. S. J. WYARD

Nemerteans

Nemerteans. By Ray Gibson. Pp. 224. (Hutchinson: London, August 1972.) £3 hardback; £1.75 paperback.

THE nemerteans are an interesting but relatively neglected group and this new book is a timely and welcome addition to the well known Hutchinson University Library Series, Much of the book is a straightforward account of what is known about the structure and biology of nemertines. In this it will prove most useful to students of invertebrates and to marine biologists and also direct attention to subjects of interest which require further study. I would have preferred structure and function to have been associated more closely than they have been. The section on the mechanics of the body wall, body shape, locomotion and hydrostatic skeleton, for example, could with advantage have been included with the descriptions of morphology. Similarly, discussion of what little is known about osmoregulation might well have been included with the account of the excretory organs, the excretory system, excretion and the origin of the freshwater and terrestrial forms which comes elsewhere. In general this divorce of structure and function is what I disliked most about this book, which does contain, nevertheless, a wealth of clearly presented information. The contents of the chapter on general physiology and many of the facts presented in the chapter on ecology should, in my view, have been included with the descriptions of structure. Although the rise in the quality of production in this series has been accompanied by a concomitant rise in price, how much better this new volume is in appearance as compared with the earliest issues in the series. Dr Gibson's drawings are excellent. There is a plate showing ultrastructural details and a colour plate illustrating *Geonemertes* (taken by Dr Batham) and the vascular system of *Malacobdella* visualized by the useful exopeptidase method done by the author.

This book will serve a useful purpose in stimulating further work on these interesting animals. R. P. DALES

Dating Man

Calibration of Hominoid Evolution: Recent Advances in Isotopic and Other Dating Methods Applicable to the Origin of Man. (Proceedings of the Symposium held at Burg Wartenstein, Austria, July 1971.) Edited by W. W. Bishop and J. A. Miller. Assisted by Sonia Cole. Pp. viii+487. (Scottish Academic Press: Edinburgh; University of Toronto: Toronto, June 1972.) (Distributed in the UK by Chatto and Windus Ltd, published for the Wenner Gren Foundation for Anthropological Research, New York.) £7.60.

THE conference of which this volume is the product was concerned with recent advances in isotopic and other dating methods and their application to dating the emergence of man. The dating technologists and geologists included Thurber, Broecker and Bender, Bandy, Miller, Fitch, Cox, Dalrymple, Fleischer and Hart, Turekian and Bada, Bishop, Van Couvering, Brown, Curtis and Hay. The palaeontologists and archaeologists were Kurtén, Walker, Cooke and Maglio, Clark Howell, Pilbeam and Isaac. Nineteen chapters are followed by discussions, commentaries and three appendices.

This book is an admirable and very topical source book for all palaeoanthropologists and archaeologists. It contains the latest dates together with new interpretations of the evidence for man's evolution. The papers are all authoritative and the whole publication amounts to an invaluable reference work. One or two well-known names which might have been included are missing, but this hardly detracts from the value of the book. The intepretation of these new dates for man's evolution has very far-reaching implications, for reliable dating is an essential basis for any logical interpretation of the fossil evidence. It will be an invaluable reference work for all who are concerned with this rapidly-growing field of study, and will allow us all to reassess our ideas about man's origin and prehistory with considerably more confidence in the hardening data of Plio-Pleistocene chronology than we have been able to muster in the past.

BERNARD CAMPBELL

Solid Optics

Optical Properties of Solids. Edited by F. Abeles. Pp. 1026. (North-Holland: Amsterdam and London, 1972.) Dfl. 200; $62.50.

This book is described on its inside cover as giving "an up-to-date account of the most recent advances in the field (optical properties of solids) . . . suitable both for graduate students and for those engaged in more advanced research". It contains eleven chapters written by various authors who have made substantial original contributions to the fields they review. Most of the articles were completed in early or mid-1968 and, in the four or five years since then, there have been many important developments which research workers cannot afford to ignore. The book will thus be primarily used as a source book for graduate and final year undergraduate courses on the optical properties of solids and perhaps also as an introduction to the field for new research workers. The editor points out in the preface that any textbook on solid state theory contains at least a few paragraphs devoted to optical properties. Sadly, most of the solid state physics tests used for final year undergraduate courses rarely do more than this and usually give virtually no account of the intrinsic optical properties of solids and the use of optical spectroscopy as a powerful tool to probe the electronic structure of both pure materials and crystal defects. This situation should improve as more books like this one become available.

The first chapter of this book gives a short review of some of the approximations used in the analysis of the optical properties of solids and this is followed by a good basic treatment of the intrinsic optical properties of semiconductors which, unfortunately, includes only three references to papers published later than 1967 and thus does not cover most of the advances made in this field during the last five years. Chapter 3, written by the editor, gives a valuable critical review of the optical properties of metals, including alloys, liquid metals and superconductors, and is much more up-to-date with even a few references to work published in 1971. This is followed by a chapter on modulated reflectance by B. O. Seraphin, a pioneer in this field, which contains a perceptive conceptual account of the relationship between intrinsic optical spectra and calculations of the electronic structure of solids. It includes a survey of the most important modulation techniques and their potential contributions to band structure analysis.

Chapters 5 and 6 give short accounts of the optical properties of non-crystalline solids and excitons respectively while chapter 7 describes magneto-optical properties of solids, principally metals and semiconductors. This is followed by a chapter on photon-photon interactions in solids which has sections on multiphonon optical transitions, anharmonic effects, alloys and the effects of impurities (but with no discussion of laser Raman spectroscopy). Chapter 9 gives a balanced review of the optical properties of colour centres in alkali halides to 1968 with 400 to 500 references. There is no discussion of related topics such as the production of colour centres by radiation and, sadly, no reference to the many interesting developments that were described at the Reading conference in 1971. This is followed by a chapter on photoemission which describes the experimental techniques needed to obtain reliable spectra and surveys experimental results on metals and semiconductors. The final chapter, on second order optical processes in solids, covers the theoretical and experimental aspects of non-linear effects such as second harmonic generation, optical mixing and so on and, finally, a section on the theory of dipole susceptibilities in perfect crystals.

In a comprehensive text of this kind one would have expected to find chapters on the intrinsic optical properties of ionic crystals, and of crystals with layer structures, the use of isotropic and anisotropic stress and, particularly, the use of synchrotron light sources to obtain information on electronic transitions involving core levels and energy states away from the forbidden gap. The chapter on excitons could well have included at least some experimental data on exciton spectra and a discussion of topics such as exciton-phonon complexes and the effects of external perturbations on exciton spectra. The rather isolated chapter on colour centres might have been accompanied by a chapter on the optical spectra of impurity ions in solids. It is sad that an expensive and comprehensive book of this kind could not be more up-to-date or, at least, that other authors did not append notes on developments to 1971 of the kind that were provided for the chapters on magneto-optical properties and photoemission. There is now a clear need for a new volume on the optical properties of solids which will also cover the progress made since 1968 and in which the principal experimental techniques (modulation, synchrotron, magneto-optic, pressure, photoemission spectroscopy and so on) are all described but in which the information obtained by all these techniques on the electronic structure of each of the different classes of materials is also described together in detail. This volume will be an authoritative and well-written source book for this future work and, in the meantime, should be a useful addition to most science libraries.

M. R. Tubbs

Polymer Structure

X-Ray Diffraction by Polymers. By M. Kakudo and N. Kasai. Pp. xii+464. (Kodansha: Tokyo; Elsevier: Amsterdam, London and New York, 1972.) Dfl. 125; $39.

The growing role of synthetic polymers in present day technology, and the realization that their useful properties depend largely on their semi-ordered molecular texture, is one of the factors that have led to the publication of books dealing specifically with the complex problems involved in the study of this texture by X-ray diffraction methods.

Another equally effective incentive is provided by the spectacular contributions of X-ray diffraction methods to our understanding of the structures of the natural polymers on which life is based; for these too are often semi-ordered. The highly ordered arrangements of molecules in crystals, and in the limited crystalline regions in polymers, are accessible by the well established methods to be found in textbooks of X-ray crystallography; but to deal in a quantitative way with the range of partially ordered textures from distorted crystalline to entirely amorphous (often in one and the same specimen), considerable extension of the mathematical treatment is necessary.

This latest contribution in this field is a translation of a recent Japanese textbook. It covers most aspects of the subject thoroughly and would provide an investigator with an adequate theoretical background for tackling the whole range of problems likely to be encountered. But it naturally has its own viewpoint which controls the treatment and the space allotted to different aspects; the emphasis is on the physics of X-ray diffraction rather than on polymer structure. It contains less information on the results of X-ray studies of molecular texture than other books of similar scope and intention published in the last few years; examples are naturally used in the exposition, but are treated only in so far as is necessary to display the methods. There is very little about the stereochemistry of polymer molecules or the relation between the properties of polymer specimens and such features as the proportion of crystalline material or the orientation of crystalline regions. This attitude is fair enough in view of the book's title, but inevitably makes it less interesting to polymer people than other books which devote more space to examples and the bearing of results on our understanding of polymer properties.

The book is divided into three sections: fundamental, experimental and analytical. It contains in its fundamental section more about the properties of X-rays than its rivals, and the development of the theory of diffraction is more complete, starting from the scattering by a single electron and proceeding to atom, to molecule and thence to assemblies of molecules. This strictly formal approach permeates the whole book, which is an impressive achievement from the mathematical physicist's point of view. The style may appeal less to some investigators than the broader approach to be found elsewhere. The diagrams, so important in this subject which deals with three-dimensional structures, are on the whole good, though some are not as clear as they might be because the elementary trick of breaking a line where it passes behind another line has not always been used. The X-ray diffraction photographs suffer by being printed on the same paper as the text; some are very poor.

The analysis of the structure of well organized crystalline regions receives little attention; although this makes the book less complete than its title implies, the omission is justified on the ground that this aspect is, on the whole, standard X-ray crystallography which is well covered in other books.

This book would be the choice, if they can afford it, of those who like a formal academic approach to the problems of semi-ordered structures.

C. W. Bunn

Laser Beams in Plasma

Laser Interaction and Related Plasma Phenomena. Edited by Helmut J. Schwarz and Heinrich Hora. Volume 2. Pp. xiv+583. (Plenum: New York and London, 1972.) $32.

Intense interest in laser fusion has been aroused recently by the declassification of some American work on the subject (*Nature*, **239**, 129; 1972). This work showed theoretically the feasibility of using laser beams to heat and compress matter to temperatures of the order 10^8 K and densities ten thousand times that of the initial solid state.

This book, dealing as it does with many of the key questions relating to laser fusion, is thus published at a very opportune time and is likely to be a best-seller. It is essentially the edited proceedings of the "Second Workshop" on the subject of laser interactions held at Rensselaer, Connecticut, in September 1971. There are thirty-eight research papers and some account of the apparently very abbreviated discussions which took place. Most of the material in these papers is now in the published literature, but it is nevertheless extremely useful to have it in a single book. Naturally the papers vary in standard and importance and the book would have benefited if some attempt had been made to show how the various aspects fit together in a summary article.

The papers are grouped in sections; in the first section on high intensity lasers there are two good papers by Beaulieu and de Maria on CO_2 lasers. But the rapid rate of progress in this field shows up here—there is, for example, no discussion of the new technique of electron beam excitation. There are half a dozen papers in the section on laser-induced breakdown, and the reader will no doubt be intrigued to discover that there is still no definitive answer to the question, "Where does the first electron come from?" In the section on diagnostics Kronast gives a good account of light-scattering experiments including a description of ways in which some more recent high resolution experiments show departures from the accepted theory.

Five papers make up the section on the interaction of laser plasmas with gases and magnetic fields. Probably the most fascinating is the account by Stamper of the spontaneous generation of magnetic fields in laser produced plasmas. A further five papers comprise the section which gives the book its title; that is, they deal with the interaction of laser light with plasma. This is possibly the most critical part of the laser fusion proposal because there is the danger that in the absence of non-classical processes the major fraction of the incoming laser light will simply be reflected. It is noteworthy that all the papers in this section are theoretical. Many of the possible non-linear absorption mechanisms are discussed here, although once again this is a subject on which new papers are appearing every week. Finally there is a section on fusion neutrons from laser-produced plasmas. This contains accounts of the much-publicized experiments in France, USSR, USA, Japan and Germany in which fusion neutrons have been detected.

In summary this book can give the near-specialist reader a very good feel for the state of the art in this subject as of late 1971.

R. J. Bickerton

Information Diffusion

Invisible Colleges: Diffusion of Knowledge in Scientific Communities. By Diana Crane. Pp. x+213. (University of Chicago: London and Chicago, 1972.) £4.05.

Although half a dozen generations have passed since it was postulated that the proper study of mankind was man, the history of science increasingly supports the postulate. Darwin placed man firmly in the animal kingdom; Freud penetrated the recesses of his motivation; tomorrow we may spell out his genius in terms of atoms and molecules. But it is only in our generation that it was realized that man might not only look at himself through the eyes of science but that he might also look in the same way at science itself.

For two centuries science and society have interacted to give us technological man but only as we seem to approach the eleventh hour are questions being asked about the *modus operandi* of scientists. These two centuries saw science evolve from being the hobby of a few score gifted amateurs into a force subvented at a cost running into thousands of millions of pounds. Many questions have been asked about this activity since Bernal and Crowther concerned themselves with the social function and relations of science.

In her book *Invisible Colleges* Professor Diana Crane, a sociologist at Johns Hopkins, has addressed herself to one of them: how is scientific knowledge generated, and how does it diffuse? The question may seem naïve but her sociometric analysis shows that an answer to the apparently simple cannot be found at the drop of a hat.

Professor Crane selected two disciplines, mathematics and rural sociology, for her studies. This may seem idiosyncratic but lacking evidence from harder sciences—say, nuclear physics or molecular biology—there is no reason to question extrapolation to these areas. Her deduction is that the social organism that promotes the expansion of knowledge is, what she calls, "the invisible college", a côterie of researchers in contact though not necessarily working together, who exercise a measure of control on the expansion of knowledge in their speciality.

The growth of science has been deemed to follow a logistic curve: a slow start, exponential expansion followed by linearity, and then, as the new knowledge is absorbed into the body of science as a whole, a final stage of stagnation or even decline. Translated into human terms this means that a small but exciting nexus sets the pace, new blood is attracted and the field is set for exponential growth both in participants and publications. Extensive and intensive activity reaps its harvest and ultimately gives way to another up-and-coming region of endeavour.

We still have a long way to go before we fully understand the social institutions that produce ideas, be they in science or the arts. Professor Crane's significant and quantitative contribution to the subject reveals the ramifications of one—her invisible colleges. Readers in a hurry will appreciate the summaries at the end of most chapters which present the wood rather than the trees, but the quick synoptic vision will only partially sweeten the pill of having to pay more than £4 for somewhat less than 150 pages of text material.

Archie Clow

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British Forests Need Lord Rothschild

THE British Government has done its best, in the past few months, to cut the figure of a resolute and hard-headed manager of research and development, eager always to balance the cost of research against the potential benefits. This, at least, is the motive for its new policy on the research councils, derived for all practical purposes from Lord Rothschild's recipe for reorganization. Given the zeal with which the campaign against the research councils has been prosecuted, however, it is unseemly that so little has been done to apply the Rothschild principles consistently. Defence research and development remain scandalously immune from tests like these. So, too, do much smaller programmes of publicly supported research, that carried out by the Forestry Commission, for example. Yet the latest annual report of the Forestry Commission (HMSO, £0.75) shows not merely that the total cost of the Forestry Commission's research increased between 1971 and 1972 by 25 per cent to a total of £1.28 million but also that this patient work, sometimes valuable, often humdrum and occasionally pointless, is undertaken on behalf of an industry whose commercial value is zero or even less.

The future of the Forestry Commission's policy on research cannot be divorced from the future of its commercial operations. In June last year, the government fired a warning shot across the commission's bows by publishing a consultative document which raised, not before time, the question of the scale on which the Forestry Commission should in future operate (*Forestry Policy*, June 1972, HMSO, £0.18). Originally, in 1919, the commission was asked to make a contribution to the strategic independence of the United Kingdom by buying land and planting trees thereon. But it has been plain, since 1958, that this is by no means a compelling justification for the continued existence of the commission—British trees at present account for only six per cent of total consumption and there are, in any case, other strategic uses that might be made of the 0.75 million hectares which the commission at present owns. This is why the government has increasingly sought to justify the commission's continued existence by saying that it is a kind of social service, providing jobs in parts of Britain where unemployment is high and the threat of depopulation is severe and, more recently, both the government and the commission have been arguing that the national forests are potentially valuable as means of recreation.

Whatever the justification for the Forestry Commission, there is no doubt that its books are in a mess. The commission functions by borrowing money from the government to finance the purchase of land and the cost of planting this with trees and has dutifully, for the past half century, kept a record of the cumulative cost of its forest building, with interest calculated at a rate which averages five per cent or thereabouts. By March 31, 1972, the total cost of forests still growing trees amounted to £405 million—a figure now recognized to be far in excess of the commercial value of the timber that will eventually be harvested. The 182,000 hectares of forest in which production had begun last March are, for example, estimated to have cost £130 million, but the commission's own estimate of the value of the timber is merely £88 million. Since the commission has used a discount rate of only five per cent in reaching this conclusion, it must be acknowledged that even this estimate of the present value of the forests is wildly optimistic—on the open market, they would not fetch a fraction of £88 million. Another way of putting this, also apparent from the commission's accounts, is to say that in the year to March 1972, it cost £5.4 million in direct expenses to harvest £7.5 million worth of wood from forests whose cumulative value was £4.5 million. In other words, as the commission has become, almost by accident, a great landowner it can make a decent return on its operations only by ignoring the cost of having grown its trees.

The consultative document *Forestry Policy*, to its credit, acknowledges that this state of affairs cannot be allowed indefinitely to persist. So far so good. But it is hard to see why the document blandly proposes that what it calls the "notional liabilities" of the Forestry Commission should now be written down to such a level that the commission will in future be able to earn three per cent a year on what will then be its investment, compared with the target of ten per cent a year fixed for most other public enterprises. For whatever the government may say about the notional character of the Forestry Commission's accounts, the truth is that the economic resources which have been forgone in the past half century are at least equal to the £404 million which represents the value of growing forests in the commission's books, may actually be more fairly represented by the £474 million given as the commission's present liabilities and would in any case be much greater if a realistic rate of interest had been charged, notionally or otherwise. If a large proportion of this capital is now to be written off, it should be openly acknowledged that the sum involved is a measure of past errors of judgment and in particular of the Forestry Commission's pigheadedly bullish view of the scale of operations which would be justified.

The government goes only some of the way to recognizing what the implications for the future should be. On the basis of a cost-benefit study carried out by government economists (*Forestry in Great Britain*, HMSO, £1.25), *Forestry Policy* says that "new planting cannot be justified by the direct and quantifiable benefits alone" and goes on to say that continued justification of the Forestry Commission's existence must depend on such things as the contribution which jobs in forestry make to preventing the depopulation of some rural parts in Britain and the value of its forests as places for recreation. The truth is, however, that providing jobs in forestry is an expensive business—the direct cost to the Exchequer ranges from £16,500 per job in Wales to £23,000 per job in the south of Scotland and is calculated to be an average of £10,000 per job in real terms (which implies making allowance for the likelihood that many of those now employed in forestry would be drawing unemployment benefit if the Forestry Commission were to vanish overnight).

In all the circumstances, it is hard to see why the government leaps blandly to the conclusion that the best policy for the years ahead is to restrict new planting of state forests to 22,000 hectares a year, with the proviso that the policy should be reviewed every three years in the light of changing employment patterns. Recognizing that the Forestry Commission's labour force of 9,055 is already dwindling, that hill farming may become substantially more profitable once the agricultural policy of the European Community comes into effect but that there are many small rural communities which have been reduced by the policies of the past half century to become dependent on forestry, a much more radical approach is called for. First, the Forestry Commission should be prevented from acquiring new land except when it can be demonstrated that a new forest will have a direct benefit on local unemployment at a cost which is supportable. It would be entirely proper to ask that the total labour force should continue to contract at five per cent a year. Second, the Forestry Commission should be instructed to sell off the forests it has grown whenever there is a chance of recovering the public money now locked up in nationalized trees. Third, the commission should be compelled to adopt the policy, advocated in the consultative document, of replanting only the most productive parts of cleared forests, letting the rest seed themselves naturally. Fourth, some means should be found of exploiting more imaginatively than the Forestry Commission can the opportunities for recreation which, after decades of devotion to impenetrable barbed wire fences, the commission now appears to recognize as its best hope of survival.

On recreation, both the commission and the government are naive, to say the best of it. The present value of the recreational value of the state forests is put at £1.5 million a year, chiefly on the basis of the amount of time which visitors at present spend in state forests and on a notional value of the amenity bestowed on them by the sight of trees. There is enough muttering in the cost/benefit analysis and the Forestry Commission's report to suggest that everybody concerned is anxious to increase the use of forests and that the Forestry Commission itself will soon start charging larger sums to those who pitch their tents overnight at authorized camping sites. An especially impenetrable report on a research project commissioned by the Forestry Commission at the University of Reading (see *Forest Research 1972*, HMSO, £1.60, also published last week) talks of "the recreational supply capability" of forests and of the "unrealized recreational potential" of the commission's holdings and promises the construction of a "recreation capability index" for half a dozen randomly selected forests. Nobody, however, seems seriously to have considered how much recreational capability potential has been destroyed, in recent decades, by the commission's policy of putting forests where people used to walk or even the commercial question of whether it might not be preferable to forget about the trees in many national forests and to turn over the land to organizations, public or private, which would manage them as recreational parks.

Against this background, the scale of the Forestry Commission's research programme is a great affront. Much of it is concerned with the collection and testing of seed and the improvement of germination, but who would suggest that even outstanding success will make the forests profitable? There is something to be said for reducing labour costs by the new techniques for planting trees developed by the research division, paradoxical though this may be if the chief justification for the forests is that they provide employment. The most interesting part of the Forestry Commission's research programme is the genetics, the physiology and pathology of forest trees, but there is a case for thinking that this could be done at least as well within the research councils and with the help of the universities, to which the Forestry Commission puts out less than two per cent of its expenditure on research. Unhappily, however, *Forestry Policy* has nothing at all to say about research. The chances are that if even Lord Rothschild were asked to say what he thinks should be done, he would find himself proposing either that the programme should be discontinued for lack of commercial justification or that the more interesting parts of it should be transferred from the Forestry Commission to the research councils on the grounds that it has very little relevance to the immediate future.

White House Muddle

THE outlook for American science and technology is gloomy. The departure of Dr Edward David from the Office of Science and Technology (see page 82) is one ominous sign of the inadequacy of the science budget for the coming financial year. President Nixon's determination to restrict the level of federal expenditure is another. The truth about the budget should be known in a few weeks, when the Administration's proposals for the financial year beginning in July will be published, although the confusion which stems from the way in which Congress's version of the Health, Education and Welfare Bill is regularly vetoed by the President will probably ensure that agencies such as the National Science Foundation will have no idea what they have to spend until the financial year is half gone. (The budget for the current year has not yet been settled.) In the long run, however, it is more serious that the Administration seems to have drifted into a muddle about its arrangements for the administration of science and technology in the United States. And, as always, it appears to have no clear idea of its objectives.

The first thing to be said, in the wake of Dr David's departure, is that it is less important, for the scientific community in the United States, that the Office of Science and Technology should be preserved in its traditional form than that the Administration should make a clear commitment to basic research and in particular to the National Science Foundation, the National Institutes of Health and to the National Aeronautics and Space Administration and the Atomic Energy Commission, which remain substantial sponsors of long-term research. For one thing, the federal government is the only means by which American universities can train graduate students and contribute to the scholarship on which the technology of the 1980s must be based. Ever since 1967, when President Johnson lightly brushed aside a demand from the National Science Board that graduate education and scholarship in science and technology should be recognized as a federal responsibility, the Administration has been shillyshallying. Agencies such as the National Science Foundation have not helped by their trendy eagerness to be more relevant, whatever that may mean. What is needed now is some mechanism by which the Administration's responsibilities for basic research can be made distinct from its other responsibilities. It is hard to see how this can be accomplished unless there is a strong coordinating body which includes the directors of the National Science Foundation and of the NIH, the research directors of the executive agencies at present supporting basic research and a strong representation from the universities.

It is also clear that the Administration is desperately in need of some means of making sense of its hitherto incoherent policies on technology. Like other governments, it has set its heart on finding means by which public expenditure can be used to stimulate industrial innovation in the civil field and to yield results of social benefit. Like other governments, it has so far failed. The difficulty has been that governments, advised by thoughtless people such as Mr William H. Magruder, have specified grand objectives and have then hoped that technologists will wave some magic wand to make cities decent, surface transport innocuous and earthquakes go away. The truth is, however, that in technology as in science, progress depends on the accumulation of small innovations whose ultimate uses cannot easily be predicted. What the American government needs is a mechanism for using the many public laboratories in the United States for maintaining a detailed watch on developments in their field of competence, for seizing new opportunities and for spending what money the government can afford. The Federal Council on Science and Technology, not a very useful body, could well be replaced by some device for controlling these activities and making sure they are sensibly directed. But here again, the Administration will have to acknowledge that it cannot make policy on its own.

Trouble in the Loch

Whatever the final outcome of the application by the Gas Council and the Total Oil Company to build a gas terminal at Crimond airport in Scotland, there are lessons to be learned—and which should have been learned a long time ago. The first thing to be said is that the application, which involves the construction of a gas processing plant on the shores of Loch Strathbeg, concerns a scientifically important site with important physical and aquatic features (see page 80 and *Nature*, **240**, 435; 1972). The second is that the terminal must be built somewhere. Britain needs North Sea gas and Scotland needs the jobs. That said, however, questions remain about the choice of site and, more important, about the way in which the provisional choice has been made public.

The site is clearly important. The Nature Conservancy says so, the Royal Society for the Protection of Birds says so and the opponents of the scheme, including Professor V. C. Wynne-Edwards, former chairman of the Natural Environment Research Council, are men of calibre, unlikely to get excited about nothing. Yet in spite of the importance of the site—and it would be naive to pretend that the Gas Council was unaware of its value—the first the Nature Conservancy officially heard of the terminal was when the Aberdeen County Council advertised on December 5 for objections to reach it within a fortnight. The conservancy, and other interested bodies, were therefore given two weeks to produce a scientific defence of a scientific site. Two months might have been more fitting.

Might not the Gas Council and Total have been somewhat freer with information about the scheme? The council says that the application was only for outline planning permission but this is a nonsense. How is it possible to tell what damage will be done until full details of the scheme are known and the likely effect on the loch accurately assessed? Similarly, Total's refusal to comment on the proposal before it went to the planning committee does not exactly encourage faith in the assumption that all other sites have been examined and that full account has been taken of the effect of the terminal on the loch. As things have turned out, Aberdeen County Council has had the good sense to postpone a decision on planning permission until fuller details are available and until the conservationists' objections can be better heard. The Gas Council and Total have this week been meeting the county council's countryside committee. Yet both the sponsors of the scheme could have saved themselves the trouble of ducking the mud thrown at them since the scheme was announced if only they had had the sense to consult other interested parties in advance.

As things are, if Crimond proves to be the only practicable site, the Gas Council and Total will have to live with the considerable hostility engendered by their handling of the matter. If some other site is finally chosen, they will somehow have to moderate the considerable distrust of conservationists in the industry's ability to consider interests other than its own. A little consultation early in the day could have saved the Gas Council and Total considerable time and effort (particularly if an inquiry holds up the application for months), and would also have avoided yet another head-on clash between conservationists and developers. Surely that is not too much to ask.

100 Years Ago

The Octopus in the Brighton Aquarium met with a sad fate on Jan. 7. Finding himself uncomfortable in a tank where he had been newly placed by the curator, he came out, in an unguarded moment, of the house of living oysters he had collected as a shelter round him. In this tank were several large specimens of spotted dog-fish. One of these fish, with the true 'cuteness of a sea-dog, immediately pounced upon the unsuspecting octopus, and swallowed him.—Another novelty has been introduced into the Brighton Aquarium, viz., the apparatus for carrying on salmon and trout hatching. The trout from the Trent are thriving splendidly.

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OLD WORLD

European Science Cut Four Ways

A FAR-REACHING reorganization of responsibilities for science and technology within the European Community has followed on the addition of Britain, Denmark and Ireland to the community.

The wide-ranging responsibilities held by Mr Altiero Spinelli until Sunday's meeting of the new commission have now been parcelled out among four commissioners. Mr Spinelli had been in charge of what were labelled industrial, technological and scientific affairs but also included a small education unit. Now Mr Spinelli is responsible only for industrial and technological affairs, and Dr Ralf Dahrendorf of West Germany, formerly commissioner for external relations and trade, has taken over scientific research matters and education. Energy policy, and those aspects of Euratom's work that affect energy policy, formerly the responsibility of Mr Wilhelm Haferkamp, now fall under Mr Henri Simonet, the Belgian commissioner, while Mr Carlo Scarascia Mugnozza, the second Italian commissioner, is to have a wide-ranging brief including environmental matters, transport and consumer interests as well as public information.

These are early days, and the full implication of the changes will not become apparent at least until the directors-general and the directors have been appointed, but it is thought that Mr Mugnozza could build for himself a powerful brief in the field loosely termed the "quality of life". But it is into Dr Ralf Dahrendorf's hands that the bulk of scientific matters now falls. He is to have responsibility for the much-troubled Joint Research Centre that is the nub of Euratom, and his first problem will come to a head on January 18, when the commission's plans for reducing Euratom's size come up again for consideration in Brussels.

The commission is acutely aware of Euratom's failings, and there is also a feeling that the JRC is too big for the job that is left for it. Fundamental research on nuclear power has suffered from the way in which national interests have set off independently in producing nuclear power plants, and the JRC, with 2,000 staff and four centres in Italy, the Netherlands, Germany and Belgium, has not enough work to keep itself occupied. Plans to move the JRC into general contract research for industry on the now familiar lines of the UKAEA's Harwell establishment fell down because Euratom's founding treaty permits virtually nothing to be done within Euratom except nuclear research.

The community is unwilling to continue funding such an expensive enterprise ($44 million in 1972), but running it down is difficult as its scientists are European civil servants. Nevertheless the commission has produced plans to close the Dutch centre at Petten which concentrates on materials testing and significantly to reduce the numbers at the Italian centre at Ispra—by far the largest of the four centres, currently employing about 1,200 people. The objective is to reduce the total staff to about 1,600. This may not be radical enough. At a meeting in December, it became apparent that the French and German governments want the staff at the JRC reduced still further to about 1,200, and the fear in the commission is that unless a compromise is reached, the JRC could be cut back so heavily that it will be unable to fulfil any useful function. Sorting out this knotty problem, not to mention the complicated financing of the centre, is now on Dr Dahrendorf's plate, although Mr Spinelli will in fact be batting for what are essentially his proposals at the January meeting.

Dr Dahrendorf is also to have the task of trying to "harmonize"—a favourite European word—the various qualifications and degrees that are earned around Europe.

The separation of science and research from technology and industry—technology apparently includes research on such matters as aerospace and computers—could improve the chances for the European Science Foundation, and could ensure a commitment to fundamental research stronger than might have been the case within a brief including technology and industry. On the face of things, Dr Dahrendorf's responsibilities for science would appear not dissimilar to the scope of activities of the British Government's Department of Education and Science.

METEOROLOGY

Cloud Seeding Attacked

IN a sweeping attack on ill-conceived attempts at weather modification, Dr B. J. Mason, Director-General of the UK Meteorological Office, has warned that the reputation of meteorology could be severely damaged and that the science could become embroiled in inter-

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CRIMOND TERMINAL

Consultation Begins

THE Gas Council and Total Oil Marine are to hold talks with the objectors to their scheme to build a gas terminal by a site of scientific importance.

Following a meeting with Aberdeen County Council's countryside committee this week, it was agreed that representatives of the industry will provide answers to specific queries about the application put to it by the committee, and that they will meet representatives of the scheme's opponents including the Environmental Liaison Group that has been set up around the university.

The proposal to build a gas terminal at Crimond airfield above Loch Strathbeg first came to light in December when the Gas Council and Total Oil Marine applied for planning permission. Fourteen days were given for objections to the scheme to reach the planning committee. In that time more than 170 objections, some of them protest petitions, reached the planning committee which decided to postpone a decision until more was known of the proposal.

Loch Strathbeg is classified as a site of scientific importance on wildlife, physical and limnological grounds, and the scheme's opponents are eager that the site should be preserved because of its international importance.

The planning committee is due to meet next on January 22, by which time the Gas Council and Total will have met the objectors to see if "safeguards can be evolved to allow the planning proposal to go ahead", according to Mr John Russell, Aberdeen's county clerk.

The key to the problem, it appears, is that the submarine relief and the nature of the sediments off the north-east coast of Scotland are among the crucial factors in deciding where the pipeline is to come ashore. One off-shore survey was completed last summer, but other surveys are still in progress and as far as Professor Kenneth Walton, professor of geography at the University of Aberdeen, is concerned "there is still not sufficient information available on which to base a firm conclusion".

national politics if such attempts continue.

In a speech to the International Cloud Physics Conference, reported in *Weather*, Dr Mason says that, "with some notable exceptions", attempts at weather modification "have generally failed to conform to the accepted principles and standards of scientific experiment and analysis, and are therefore incapable of providing objective answers to such questions as to whether, in what circumstances, and to what extent it is possible to modify precipitation by artificial seeding. . . . Politicians and entrepreneurs are initiating and conducting major weather modification projects without the benefit of proper scientific direction, advice and criticism, and this may have serious repercussions on the reputation of meteorology as a science and profession".

Dr Mason went on to complain "that such operations are being promoted on the assumption that the basic assumptions and techniques are already proven and that the remaining problems are largely of an engineering or logistic nature". But in fact "the protagonists of this approach are continuing to use the same inadequate concepts and techniques that have failed to provide convincing answers during the past twenty years".

"We hardly begin to understand the processes that control the intensity, durability and distribution of precipitation as witnessed by our evident inability to predict these quantities within fifty per cent, even for short periods—shorter than the lifetime of the storm. . . . This leads me to challenge the thesis that weather modification is the main practical justification for cloud physics research and to suggest that, taken world-wide, the potential economic and social benefits of accurate prediction of precipitation outweigh those of modification for the foreseeable future".

Dr Mason went on to say that while, in emergencies, weather modification might be attempted in the hope of ending severe droughts, a sharp distinction should be drawn between such operations and carefully designed experiments "that have some chance of producing answers to properly formulated scientific questions".

The international implications of weather modification also alarm Dr Mason. Suggestions that the World Meteorological Organization should advise the developing world on cloud seeding should be treated with caution. Such advice should not be given until thorough on-the-spot investigations of local conditions had been completed, and even then "an advanced country should consider very carefully the wisdom of urging on a developing country largely unproven techniques".

According to Dr Mason, Project Whitetop, one of the few well designed weather modification programmes, in which Missouri clouds have been seeded with silver iodide for a five-year period, suggests that rainfall actually decreased between 40 and 60 per cent in the 100 miles downwind of seeding, although there may have been some increase 180 miles downwind.

Dr Mason is also concerned that if weather modification does become feasible on a large scale, "an ill-judged attempt by any nation to carry out such a project without international agreement would, almost certainly, plunge meteorology into the cockpit of international politics, controversy and dissension". The effect on programmes such as the World Weather Watch and the Global Atmospheric Research Programme could be disastrous, Dr Mason says.

His solution is that meteorologists should, through learned societies, scan weather modification programmes carefully and "grant scientific recognition and approval only to those that fulfil rather strict scientific criteria, have scientific direction and are open to inspection and evaluation by independent scientists". Projects that are not vetted should not be eligible for presentation at scientific meetings or for publication in scientific journals. Dr Mason admitted this week that such a proposal might be labelled as censorship, but he argued that the situation is potentially so serious that the profession must safeguard its scientific integrity.

SOVIET SCIENCE

Vavilov Commemorated

from our Soviet Correspondent

THE Soviet Ministry of Communications has issued a special commemorative envelope to mark the thirtieth anniversary of the death of Academician Nikolai Ivanovich Vavilov, "the Soviet botanist, geneticist and selectionist", thus marking a further stage in the rehabilitation of the leader of the anti-Lysenko conflict of the 1930s.

Vavilov, whose outstanding services to Soviet agriculture in crop breeding and genetic selection are beyond dispute, was arrested in July 1941 on a number of charges ranging from "sabotage in agriculture" to "spying for England" and "belonging to a rightist conspiracy". His real offence, however, was his opposition to Stalin's sponsorship of the theories of Lysenko. Vavilov was sentenced to death and, although the sentence was later commuted to ten years imprisonment, he died in Saratov prison on January 26, 1943.

Vavilov was posthumously rehabilitated by the Soviet Supreme Court on September 2, 1955. A week later, the praesidium of the Academy of Sciences restored his name to the register of deceased members. Since then the rehabilitation process has gone slowly and tacitly forward. In 1960 a Vavilov memorial volume was published. Articles praising his work have appeared from time to time in the Soviet press. November 26, 1971, the 84th anniversary of his birth, was marked by the unveiling of a memorial plaque on the wall of the Institute of Genetics in Moscow.

SPACE RESEARCH

Astrophysics Unit Moves

THE Science Research Council's Astrophysics Research Unit has been transferred to the council's Radio and Space Research Station at Slough. This transfer, effective from January 1, adds a strong astrophysical side to the support work already carried out by the station.

RSRS is the SRC's chief support centre for university space research, and currently provides such services as prediction satellite orbits, environmental testing of space experiments and provision of data centres for rocket, satellite, ionospheric and solar data. The station also provides support for radio astronomers, and the SRC's Space Research Management Unit which plans rocket and satellite programmes is there.

This supportive role for Slough emerged from an SRC panel report on the station in May 1971, and the addition of the astrophysical unit means that most SRC support of university space work can now come from one centre.

The decision to move the unit ensures its continuity which was very much in question following an examination, in 1968, of the work of the United Kingdom Atomic Energy Authority's Culham laboratory of which the unit was a part. At the time it was suggested that the unit might be disbanded, but the SRC took control and its work on solar physics, laboratory astrophysics and ultra-violet astronomy continued, with the unit still at Culham.

A large part of the unit's work already involves collaboration with university work, so its new role will not be a radical change of direction. Although the unit is now under the control of Dr J. A. Saxton, the director of RSRS, and is now one of the station's divisions rather than an organization in its own right, the unit's staff of forty will not be moving to Slough for some time. Extra accommodation will have to be provided before a physical move can actually take place.

Dr R. Wilson, who was director of the astrophysics unit, has now moved to University College, London, to take the post of Perren Professor of Astronomy.

NEW WORLD

David Resigns, Changes in the Offing

by our Washington Correspondent

DR EDWARD E. DAVID, JUN., sprang a surprise last week by resigning as Director of the Office of Science and Technology and Science Adviser to the President. He told his staff soon after the new year's holiday and later that day flew to Chicago to take up his new job as executive Vice-President of Gould Inc., a manufacturer of electrical and electronic equipment. No successor has yet been announced and, indeed, the big question is whether or not David will be replaced, for his departure has intensified speculation that the science policy machinery in the White House may be drastically reorganized.

David's resignation was accompanied by the expressions of regret and thanks from the President which are usual on such occasions, and he has said himself that he is not leaving because of any dispute or with any sense of disappointment. Indeed, there is nothing extraordinary in his serving only two years of what is, on paper, a six year term of office—there have been six science advisers since the job was created.

David's departure has nevertheless prompted speculation that he has quit because his advice too often fell on deaf ears. This suggestion was played down by some White House officials last week, but others did not deny the possibility. One ominous possibility is that his departure is linked with the negotiations on the science budget for 1974, now almost complete.

It is generally accepted that this will be tightly squeezed. A recent study by the Brookings Institution suggested, for example, that in order to meet his goal of keeping federal expenditure below $250,000 million, President Nixon must cut some $7,000 million from present expenditures. Although science and technology accounts for only a relatively small part of the budget, it unfortunately falls into the category which is cuttable—all but about $72,000 million of federal expenditures are earmarked for items such as social security and pensions which cannot be reduced.

Whatever the reasons for David's departure, it cannot be denied that it was kept a closely-guarded secret. One White House official said last week, for example, that "although some of us knew he was thinking of leaving, few of us thought he would do it". The news of his impending departure had also not reached the President's Science Advisory Committee (PSAC), of which David was chairman.

An electronics engineer who spent 20 years working for Bell Laboratories Inc. before joining the White House in 1970, David was Science Adviser to the President during a particularly difficult time. He was appointed when expenditures on science and technology were declining, and lived through some tricky political negotiations over the federal government's plans to stimulate industrial research and development and to bring science and technology to bear on domestic problems. Throughout his tenure of office, he sensibly kept "a low profile", which makes it difficult for outsiders to judge his effectiveness, but he is widely respected in the scientific community. During the past two years, expenditures on science and technology have even shown a modest increase.

David's most difficult time was in 1971, when Mr William Magruder was brought into the White House to take charge of what was called the "New Technology Opportunities Program" (NTOP). The idea was to find ways to stimulate industrial research and development and to plan new opportunities for using science and technology to solve problems such as pollution control and urban decay. Magruder's appointment was viewed as a slap in the face for OST, and his approach, as characterized by Dr Lewis Branscomb in a speech given at the AAAS last month, was to argue for large federally funded projects. The outcome could be seen in the President's Message on Science and Technology, which outlined a policy base, but included few big projects. David emerged relatively unscathed from that process, and the OST's political influence was, if anything, increased.

Now that David has departed, what lies in store for the OST and PSAC? The first thing to be said is that the post of Science Adviser to the President and PSAC itself were both set up by the President in 1957, and the Office of Science and Technology was established in 1962 by an Executive Reorganization Plan. None of them, therefore, has a Congressional charter, and all could be scrapped by the President without the consent of Congress. It would thus seem logical that if changes are in store for the White House science policy machinery, this would be a good opportunity. But, as one White House official remarked last week, "that assumes that we do things logically, which is a big assumption".

The most common view appears to be that OST is likely to be tied in more closely with the Office of Management and Budget, chiefly on the grounds that such an arrangement would allow it to give more direct support to the Nixon Administration's general philosophy that science and technology must be supported on the basis of their possible payoffs in economic growth and socially useful innovations. Relevance is the watchword. Although OST has always given advice on the budget as it relates to science and technology, its relationship with OMB has been obscure.

As for PSAC, no action had been taken at the end of last week on its pro-forma resignations which the members submitted after the election, but two recent events suggest that President Nixon does not think much of the committee. First, it took seven months to fill three vacancies on PSAC—the terms of office of three members expired on December 31, 1971, and they were not replaced until August 1972. Second, the Administration is embarrassed by a PSAC report on the SST. Called the Garwin Report, it was critical of the SST project at a time when the Administration was backing the project, and although it was meant to be secret, its recommendation that the government should withdraw support from the SST prototype leaked out. Eventually, after a lengthy court battle, the OST released the report. If President Nixon does intend to scrap or modify PSAC, however, his plans have not been disclosed to the committee's members.

OST and PSAC are not alone in their anxiety about the future. At the end of last week, four other key scientific posts were unfilled. No successor to Dr James Schlesinger, who is being moved from the chairmanship of the AEC to become Director of the CIA, had been announced. There are also vacancies at the head of NIH, at the Department of Health, Education and Welfare, where Dr Merlin K. DuVal recently resigned as Assistant Secretary for Health, and in the Department of Defense, where Dr John S. Foster Jun. is resigning as Director of Defense, Research and Engineering.

Whatever arrangements the Administration makes, it is likely to find itself embroiled with Congress on several fronts, not least on the question of whether Congress or the White House holds the pursestrings. With Democratic control of the Senate strengthened, with the past year's record of occasions on which the White House has withheld funds appropriated by Congress and under the stimulus of protest at the renewed bombing of Vietnam, many members of Congress are up in arms about the constitutionality of the Administration's relationship with the Capitol.

Last week, for example, seventeen senators, including the chairmen of thirteen committees, majority leader Mike Mansfield and majority whip Robert Byrd joined with the state of Missouri in a suit against the Administration which alleges that the withholding of highway trust funds last year was illegal. A federal judge ruled in favour of the state last year, but the Administration has appealed. And a bill has now been introduced by Senator Sam Ervin, chairman of the Senate Government Operations Committee, which would require the President to inform Congress thirty days before any funds are impounded, thus allowing his decision to be overridden.

The debate on the pursestrings is important to science and technology because the Administration is expected to withhold between $6,000 and $10,000 million of the money appropriated by Congress for projects in the 1973 fiscal year, now more than half way through (see *Nature*, **240**, 247 ; 1972).

Congress and the Administration are also likely to be at odds over a specific piece of legislation involving science policy—Senator Kennedy's National Science Policy and Priorities Act. Passed last year by the Senate by a vote of 70–8, the bill failed to emerge from the House Committee on Science and Astronautics before the 92nd Congress dispersed. It was, however, introduced again by Kennedy last week, and stands a good chance of passing through the Congressional mill this session. President Nixon would, however, be certain to veto the bill because it calls not only for $1,800 million to be spent over three years on research and development directed towards domestic problems and on retraining unemployed scientists but also for expenditures on research and development to increase faster than the gross national product.

In the more immediate future, Congress must conjure up an appropriations bill for the Department of Health, Education and Welfare which is acceptable to President Nixon. Although the 1973 fiscal year started on July 1, 1972, NIH and the other agencies in HEW are having to make do with the same level of funding they received last year, because Nixon twice vetoed 1973 HEW appropriations which he considered excessive. Congress can be fairly certain, however, that the Administration will impound any funds which are added on to its 1973 budget request for HEW. The fight for control of the pursestrings will thus be followed with close attention.

All Aboard

One of the first acts of the 93rd Congress was to appoint Senator Clifford Case to the board of the Office of Technology Assessment and to confirm that Senator Edward M. Kennedy will be the board's first chairman. In addition, Olin Teague of Texas, the new chairman of the House Committee on Science and Astronautics, is expected to be given the place vacated by the departure from Congress of Earle Cabell. Senator Case, a Liberal Republican from New Jersey, replaces Senator Gordon Allott. Allott and Cabell both lost their seats in Congress in the November elections.

The new board is, however, having some difficulty in getting together—all twelve members must be present for the first meeting so that a quorum can be fixed—and the first session is unlikely to be before the end of the month. And it will be April at least before the office gets under way, for the director and staff cannot be appointed until funds are made available by the appropriations committees. Although the bill which established the office authorized $5 million to start it up, the money will not be available until a supplemental appropriations bill has gone through Congress, probably lumped in with other supplemental appropriations in the spring.

NASA

HEAO Shelved

by our Washington Correspondent

The National Aeronautics and Space Administration announced last week that it has halted work on the High Energy Astronomy Observatory (HEAO) and on nuclear propulsion, that it is phasing out research and development on communications satellites, and sharply curtailing work on nuclear power. These casualties are direct consequences of President Nixon's campaign to hold federal spending down to $250,000 million this fiscal year, and they indicate that NASA will be particularly hard hit by budget cuts.

Work on HEAO has been suspended for at least a year, while NASA officials study "ways to meet some of HEAO's objectives at lower costs", which is being interpreted to mean that the satellite has been shelved, at least until the space shuttle is available to put it into orbit. The news has been greeted with bitterness by astronomers, who regard it as perhaps the most important satellite planned by NASA—it has consistently been given the highest priority by the Space Science Board of the National Academy of Sciences, for example.

NASA officials decided to apply the knife to HEAO rather than to other expensive projects for two reasons. Not much money will be wasted if it is scrapped, because the project is only just getting under way, and it is not tied to a launch date because it will be placed into Earth orbit. Only about $18 million have been spent out of a total estimated cost of $250 million for the project. Scrapping HEAO will, however, severely stunt the growth of high energy astronomy because although rockets, balloons and small satellites can be used for high energy experiments, heavy instrumentation is required for high sensitivity and resolution. So far, two high energy astronomy satellites have been launched—an X-ray astronomy satellite and a gamma ray astronomy satellite—and another satellite to study soft X-rays is scheduled for launch in 1975. Astronomers are now hoping that some of the experiments planned for HEAO can be flown on smaller and less expensive satellites.

As for communications satellites, NASA officials have decided that they should now be developed by industry. NASA has provided the initial costs of research and development on communications satellites, and the agency will launch the next in the series, ATS-F, in 1974. All work on ATS-G has, however, been stopped.

The decision to scrap research and development on nuclear propulsion and to curtail work on nuclear power systems was taken because "all prospective applications are in the very distant future". NASA in fact decided a year ago to scrap its development of a large nuclear rocket, and to concentrate on a smaller system, but that decision was greeted with some distaste, especially in Congress (see *Nature*, **235**, 415; 1972). The decision to scrap all development of nuclear propulsion will, however, be more widely criticized because planetary scientists were hoping that nuclear engines would be capable of taking spacecraft to the outermost planets in the late 1980s. Without the Grand Tour and nuclear rockets, the outer planets are likely to be out of reach at least this century.

Although the cuts announced last week were made to save money in the present fiscal year, they provide some pointers to NASA's plans for 1974. The Viking mission to make a soft landing on Mars is likely to go ahead, for example, otherwise it would also have been scrapped now to make the maximum savings. Similarly, hopes are high that the Mariner mission to Jupiter and Saturn will be saved from the axe. But as late as the end of last week, NASA officials were still engaged in hard bargaining with the Office of Management and Budget. At least one project is being dealt with lightly: the space shuttle has had only minor cuts in manpower build-up, and it will certainly go ahead.

SENATE COMMITTEE

No Fight for Space

THE Senate Democratic leadership sprung a surprise last week by appointing Senator Frank E. Moss of Utah to the chairmanship of the Committee on Aeronautical and Space Sciences. Moss, a widely respected Senator who was first elected in 1958, has never been a member of the committee. Although he has consistently voted in favour of the space programme, he has not shown an unusual amount of interest in space affairs. His appointment came about because none of the members of the committee who were in line for the chairmanship wanted the job.

The chairmanship of the space committee, vacant because of the retirement last year of Senator Clinton P. Anderson, a founder member of the committee, would normally have been passed to Senator Warren Magnuson. Understandably, however, Magnuson preferred to hang on to the chairmanship of the more powerful Commerce Committee, and the offer went to Senator Stuart Symington. But he said last week that his commitments on the Armed Services Committee, the Foreign Relations Committee and the Joint Committee on Atomic Energy are more than enough to keep him occupied. The next in line, Senator Howard Cannon of Nevada, has chosen to hang on to his chairmanship of the Rules Committee. Their reluctance to take on the chairmanship of the space committee is a good measure of the decline in the committee's importance.

NIH

Fallout from Marston

by our Washington Correspondent

THE forced resignation of Dr Robert Q. Marston as Director of the National Institutes of Health (see *Nature*, **240**, 437; 1972) has sparked off a wave of protests from scientists at NIH itself. The reasons why President Nixon accepted Dr Marston's *pro forma* resignation have not been spelled out and a successor has not yet been nominated, but it is widely felt that Marston's resignation was brought about for political reasons, and that he will be replaced by someone closer to the Administration. One view is that Dr Marston has paid for not having fought hard enough for the Administration's cancer bill, which would effectively have taken cancer research outside NIH.

The Inter-Assembly Council of the Assemblies of Scientists, which represents professional scientists at NIH, wrote last week to the President to complain that this is the first time that a director of the NIH has been made to resign after a presidential election, to urge that Dr Marston has done a good job and to hope that his successor will be a person of stature in research, not merely an administrator.

AAAS

Genetics, Good or Bad

by our Special Correspondent

THE Youth Council of the AAAS provided some spirited discussion at its December meeting of the legal and sociological implications of one branch of science by a symposium on genetics, man and society. Organized jointly with the Yale University Task Force on Genetics and Reproduction, the meeting aired many diverse points of view, not only from the expert members of four inter-disciplinary panels but also from the lively audience.

About half the allotted day was devoted to talk of screening and genetic counselling programmes. Obvious though the advantages of being able to predict before birth that a child will be afflicted with a crippling disease such as muscular dystrophy may seem, there is room for heated argument. For example, the recently introduced requirements of some states and municipalities that members of the black population should be screened for sickle cell anaemia have sparked off great controversy which was reflected in the opinions expressed at the symposium. Thus Dr H. A. Bender, a biologist from the University of Notre Dame, suggested that critics of this programme are foolishly asking for the right not to know about their genetic problems. This, he said, may have incalculable costs but consequences such as harsher insurance rates or diminished opportunities of employment for people whose sickle-cell trait has been detected stem from the failure of scientists to educate the population properly. By contrast, Dr I. Ladimer, a physician and lawyer from Mount Sinai School of Medicine, suggested that the sickle cell anaemia screening programme is unethical so long as there is no really effective therapy available.

On *in vitro* fertilization and the subsequent culture of human oocytes, one view at this meeting was that the technique may be valuable for women who are infertile because their oviducts are blocked. Dr B. G. Brackett, who is engaged in this work at the University of Pennsylvania, felt that in spite of the present technical barriers, it will eventually become possible to implant fertilized ova in such women.

On the question of legislative measures to regulate the use of genetic knowledge, Mr H. Jasper, a legislative assistant to Senator W. F. Mondale, pointed out that probably only four or five senators and even fewer representatives know more about genetics than the lay public. He advocated action now to establish a framework for policy-making, rather than to wait until a disaster prompts the hasty passage of specific and poor legislation. The former course is implicit in Senator Mondale's proposal for a public advisory commission to make a two-year study of the ethical aspects of biology included in the bill he steered through the Senate last year but which eventually died in a House committee room.

Change at the Top

by our Washington Correspondent

RESIGNATIONS and appointments for natural causes still take place in Washington. Dr Rocco A. Petrone, Director of the Apollo Programme, will become director of the Marshall Spaceflight Center in succession to Dr Eberhard Rees, who retires on January 19, and George Vineyard jun. has been chosen to succeed Dr Maurice Goldhaber as director of the Brookhaven National Laboratory. Dr Goldhaber is returning to full-time research.

The announcement of Rees's retirement and Petrone's appointment was neatly stage-managed to coincide with the end of the Apollo programme, in which both played a significant part. Petrone had directed the programme since September 1969, while the Marshall Spaceflight Center has been responsible for the Saturn Launch vehicle and the development of the Lunar Rover. Rees was deputy director of the center from 1960 until he succeeded Dr Werner Von Braun in 1970.

The new chief at Brookhaven has been deputy director for the past five years. A solid-state physicist, he takes on his new job when Brookhaven is diversifying into such fields as the environmental effects of various types of energy generation. But his chief headache will be the continuing shortage of funds for high-energy physics, particularly in relation to Brookhaven's proposal for a new colliding-beam device.

NEWS AND VIEWS

How Useful is Earthquake Prediction?

FOR many years seismologists have been measuring the velocity of compressional (P) and shear (S) waves in rocks and studying the relationship between these velocities and the elastic moduli and density. These parameters can change with changes in the applied stress; before an earthquake occurs the stress in the focal region increases, and if this increase can be monitored it may lead to a method for predicting the onset of the elastic failure responsible for earthquakes. Attempts to monitor P and S velocities in the past, using explosive charges over a measured line, never came to anything, and interest in this type of experiment waned. That was until 1969, when Semyenov published the results of an experiment in the seismic area of Garm in the Soviet Union (*Izv. Phys. Sol. Earth*, **4**, 245 ; 1969). Semyenov showed that, before an earthquake with a value of m_b of the order 4 or more, there is a significant variation in the ratio of the P and S velocities. He reported observations of microearthquakes in the Garm region which showed that the ratio $v_p v_s$ remained fairly constant at about 1.77 ± 0.01 for considerable periods of time before $v_p v_s$ began to decrease to a minimum value of less than 1.70 followed by a sharp increase before a larger earthquake.

On page 101 of this issue of *Nature* a significant confirmation of these Soviet results is reported by Aggarwal and his colleagues of the Lamont–Doherty Geological Observatory. The significance of their work is that they have repeated the Soviet experiment in a completely different region of the Earth, namely the Blue Mountain Lake area of New York State, and have obtained very similar results. They, too, used microearthquakes as an energy source to monitor and establish the norm of the $v_p v_s$ ratio. In the Blue Mountain Lake area, they deployed a network of high gain seismograph stations, which were sufficiently close to obtain hypocentre information with adequate precision. Although no seismograms are illustrated in the article whereby the reader can judge how precisely the onsets of the P and S waves can be measured, the authors affirm that these arrivals are very clear and impulsive and can be read consistently to an accuracy of 0.01 s. Certainly the data show very little scatter, and as in Garm the ratio v_p/v_s decreases to a minimum and increases sharply before an earthquake.

Why should the ratio v_p/v_s vary in this way when an earthquake is about to occur? Nur has attempted to explain the Soviet observations by suggesting (*Bull. Seism. Soc. Amer.*, **62**, 5 ; 1972) that the decrease in the ratio may be the result of dilatancy, that is to say decreased volumetric strain, of rocks in the focal region as a consequence of increased stress. The sharp increase in the ratio just before the earthquake may, he suggested, be caused by the flow of ground water into cracks formed by dilatancy. Increasing the pore pressure in this way weakens the rocks. A similar interpretation is presented by Aggarwal *et al.* in their article.

This hypothesis is also used to explain the increased seismic activity observed in Colorado when effluent fluids were pumped into deep boreholes. The increased seismicity around new dam and reservoir sites is similarly explained ; further development of the idea should come from seismographs now commonly installed around new reservoir sites. At these sites the experiment can be carried out at all stages of construction before and after the reservoir is filled.

What does this technique contribute to the art of earthquake prediction? For the present it would seem very little, for it remains to be seen whether or not the observations are caused by shallow and superficial phenomena. The observed variation in the velocity ratio would seem to be very local and is a precursor to very small and particularly shallow earthquakes (about 3.5 km). The costs of the comprehensive network of stations which would be required for monitoring, their operation and the continuous processing of the data are far from trivial. Other observations of geophysical changes preceding an earthquake, such as small changes in the electrical conductivity of the rocks and variations in radon exhalation as the rock is stressed, are similarly localized and would suffer from similar logistic problems if they were to be applied in an operational sense.

It is also worth drawing attention in this context to the tendency for the more scientifically interesting problems associated with earthquake prediction and control to obscure the fact that the application of well-known civil engineering methods would mitigate the loss of property and life in cities, and for the more useful, if less glamorous, projects concerned with the problem of well-insulated, low-cost housing for villages in seismic areas to be starved of funds. There is little to be gained by predicting earthquakes, such as the one which recently hit Managua, if afterwards there is no city to which the temporarily evacuated inhabitants may return.—From a Correspondent.

Synthesizing Diamonds

PRECIOUS stones must satisfy two criteria—they have to sparkle and they have to be hard. Diamond, being the hardest material known and possessing a high refractive index and good dispersion, obviously qualifies ; but in addition it has one property of even greater value for the world at large—it is not found in significant quantities in the United States.

For this reason the decision was taken in 1951 to "mount a major new assault on the old and bloody battlefield" of diamond synthesis ; the US General Electric

Company announced success on February 15, 1955, and in 1960 Dr Guy Suits described this operation in an article entitled "The Synthesis of Diamond—A Case History in Modern Science", written, as he explained, because "traditionally, the history of political events and warfare between nations is recorded in minute detail . . . But we have not yet established a tradition of recording in historical detail the events of science and technology, which are increasingly playing a decisive role in human welfare and the affairs of nations". The point is illustrated by his observation that "the ultrahigh pressure, high temperature process for forming diamonds, which at first strained existing high pressure technique almost to its limits, has in only a few years become a routine production process which has turned out millions of carats of diamonds. As a result, this country [the United States] has been relieved of a critical dependence on industrial diamonds from the Congo".

The diamond project was not cheap (I think I first heard the word "megabuck" in connexion with diamond synthesis). One reason, as Dr Suits explains, was that so much exploratory work had to be done, and blind alleys and detours absorbed almost as much human energy as the successful portion of the project. One had to be very careful about jumping to conclusions ; as one of the team wrote in his notebook: "In each sample I found many absolutely perfect octahedrons . . . They certainly look like the real thing . . .", but they were subsequently found to be chromite, originating in the chromium of the stainless steel reaction chamber. Nor did the development of apparatus always proceed smoothly ; it was soon found that gaskets made from the pipestone of the American Indians, as used in the pioneer high-pressure experiments of Bridgman (and selected for him by one particular Indian in the best traditions of alchemy), had to be abandoned in favour of the much less romantic but far more satisfactory material, pyrophyllite. Above all, "the measurement of pressure and temperature in the original cell, and all subsequent cells, turned out to be a continuing source of difficulty and uncertainty".

Neither was it easy to learn from natural diamond. In 1952 attempts were made to establish the graphite-diamond equilibrium curve experimentally by graphitizing diamond, but "unexpectedly, determination of the onset of graphitization proved to be difficult. Different diamonds behaved differently. Some showed surface blackening, some became smoky, and some remained clear and resisted graphitization even at relatively high temperatures". These remarks emphasize that in diamond research the concept of the "average diamond" is about as useful as that of the "average Briton" for all but the most trivial investigations.

But General Electric persevered with the synthesis experiments, and eventually found that iron sulphide in a graphite tube with tantalum end-disks produced diamonds ; in fact many metals could be used, provided that the temperature was high enough to melt the metal when saturated with carbon. Much of their work was summarized in a communication in *Nature* (**184**, 1094 ; 1959), and in 1960 Dr Suits could write, "With a great range of experimental conditions available through a choice of temperature, pressure, catalyst-solvent and time, it is not surprising that the size, crystal habit, colour, clarity and other properties of man-made diamonds are subject to a significant degree of control. Diamond can be grown for specific industrial applications. . .".

If the Congo suffered as a result of this work, geophysics did not. The impact of this achievement can be seen very clearly in the opening pages of the Annual Reports of the Director of the Geophysical Laboratory in Washington. Already in 1956–57 the report says that "when equipment currently under development is operable, this laboratory will be able to participate very actively in advancing one of man's great frontiers—high pressure studies". In 1957–58 it points out that "knowledge of the mineral constitution of the upper mantle and of the deeper parts of the Earth's crust is fundamental to progress in many fields of geophysics and petrology . . . Interpretation of seismic discontinuities and working out the origins of rocks such as eclogites, kimberlites and granulites are only a few of the problems whose solutions depend . . . on our knowledge of mineral equilibria at greath depth. Progress in this field depends directly on our ability to duplicate in the laboratory the conditions of high pressure and temperature that exist at depth in the Earth". In 1959–60 the report actually begins: "Results of fundamental research frequently are universally applicable. Knowledge of phase equilibria in silica and sulphide systems gained at the Geophysical Laboratory has repeatedly been applied to mineral association in rocks from all the continents and to meteorites. Application of our work is likely to be extended further, since personnel of this laboratory are currently participating in the planning phases of two new frontiers of earth and planetary science—the space program and the Mohole project". In 1965–66 one reads that "progress in science is often contingent on the development of new apparatus. This is especially true in a field such as high pressure research in which workers are continually seeking means of studying phenomena under ever more intensive conditions".

While the geologists were revelling in the new possibilities opened up by the advent of successful high pressure technology, the scientists at General Electric had not been idle. They succeeded in growing gem diamonds in a variety of colours with shapes so reminiscent of the well known emerald cut that acceptable gems could be obtained from them without significant loss of weight on cutting—a very important bonus when the weight loss involved in faceting natural diamonds is seen by comparison—and there can be little doubt that the technological problem of synthesizing large diamonds has been solved, although not yet as an economically viable process ; it is still cheaper to dig them up.

Commercially valuable processes of this kind are normally protected by patents, and, predictably, the advent of synthetic diamond production in Sweden, South Africa, Japan and the Soviet Union brought headaches for the interested parties. It is in this context that the experiments described by Francis Bundy on page 116 of this issue of *Nature* will arouse concern. At what percentage, one may ask, does a contaminant become a constituent? The communication emphasizes the serious problems which still beset workers in the high pressure field, and the prime importance of painstaking experimentation. The pre-eminent position of General Electric in this field for the past twenty years must ensure that their results are taken seriously.

The fact that traces of nickel may be decisive for diamond synthesis is of interest also in the geological context, because although all can study pieces of the

Moon, the Mohole project has not yet delivered a stick of upper mantle rock. Some of the best preserved mineral grains available to geologists at the present time from high pressure environments are in fact the crystalline inclusions in diamond; the commonest of these inclusions is olivine, and six olivines (three from Venezuela and three from Ghana) microprobed at the Geophysical Laboratory in Washington showed not only an extremely constant ratio Fe/Mg (about 8 per cent Fe), but also an extremely constant Ni content, at about 5 per cent of the Fe content. As the 1959 paper put it, "diamond can form in several different ways, and stubborn mysteries still surround some of them". Diamonds aside, geologists as a whole owe much to General Electric. Maybe it is time that somebody named a new mineral for them.
—H. J. M.

Sequencing DNA

Methods, notably those devised and developed during the past several years by Sanger's group at the MRC Laboratory of Molecular Biology in Cambridge, which allow the determination of the nucleotide sequences of RNA molecules have become part of the stock in trade of molecular biology laboratories. Announcements of the determination of the complete base sequence of this or that transfer RNA or other small RNA molecule have thus become almost commonplace and cause only a ripple of general interest, although messenger RNA molecules, whose sequences molecular biologists would dearly like to know, cannot usually be purified to the standards required for sequence analysis. In short, the methodology for sequencing RNA molecules is at hand and the chief obstacles to analysing many interesting RNA molecules lie in their purification.

By contrast, methods for analysing the base sequences of DNA molecules are still in their early infancy and most groups intent on determining the nucleotide sequence of short fragments of DNA have shirked taking the bull by the horns and have instead adopted indirect approaches. Usually these methods involve either transcribing *in vitro* with *Escherichia coli* RNA polymerase the DNA of interest and then analysing the base sequence of the RNA transcript, or using *E. coli* DNA polymerase I to synthesize a labelled complementary DNA chain which can be analysed. The obvious disadvantage of these sorts of experiments is that they rely on the fidelity of *in vitro* transcription or DNA synthesis, which is not the least of the reasons why Sanger and his colleagues have tackled the problem of devising a generally applicable methodology for the direct analysis of the base sequences of DNAs. To judge from what Ziff *et al.* and Robertson *et al.* had to say in last Wednesday's *Nature New Biology* (**241**, 34 and 38; 1973) they have succeeded in their objective.

The first problem facing anybody who tries to analyse the base sequence of a naturally occurring DNA molecule is that of devising methods for partially digesting the DNA into specific fragments small enough to analyse; the smallest DNAs, phage genomes, are at least 5,000 bases long. Ziff *et al.* used T4 phage endonuclease, which preferentially attacks single-stranded DNA, to digest partially single-stranded ϕX174 DNA in conditions which favour the formation of DNA secondary structure. They then separated by gel electrophoresis the fragments of ϕX174 DNA, which because of the specificity of T4 endonuclease have a 5′ cytidine residue bearing a 5′ phosphate group and isolated two for further analysis. Robertson *et al.*, on the other hand, used a technique devised by Steitz for the sequence analysis of the ribosome binding sites of phage R17 RNA to obtain a fragment of ϕX174 DNA. They bound 70S ribosomes to the single-stranded ϕX174 DNA, using conditions Bretscher had devised to bind ribosomes to DNA, and then they digested away all the ϕX174 DNA that was not protected by the bound ribosomes. The ribosomes were then dissociated and the protected fragments of DNA released were then subjected to gel electrophoresis and chromatography. The population of fragments of DNA proved to comprise one large portion about fifty nucleotides long and several smaller portions; the principal portion was isolated for further analysis. Clearly both these methods for obtaining small fragments of DNA have their limitations and no doubt in the future enzymes such as the bacterial restriction endonucleases, which can cut double-stranded DNA at specific sites, will be used by DNA sequencers.

Having obtained a fragment of ϕX174 DNA of manageable size, Ziff *et al.* began the task of analysing its sequence. The procedure which they devised involves depurination and further digestion of the fragment with T4 endonuclease, snake venom phosphodiesterase and spleen phosphodiesterase coupled with standard fingerprinting chromatography. Using these procedures the group obtained the base sequences of a series of overlapping oligonucleotides and hence the sequence of the forty-eight nucleotides in the fragment of ϕX174 DNA.

By exploiting these procedures and in addition using streptococcal nuclease Robertson *et al.* determined the sequence of the fifty-one bases of the strong ribosome binding site in ΦX174 DNA which they had isolated. This sequence is interesting because it contains an ATG triplet which is, of course, the equivalent of an AUG codon in messenger RNA. Furthermore, if the base sequence is read in triplets, starting with the ATG triplet, an amino-acid sequence can be predicted. This predicted sequence is identical to that at the amino-terminal end of the ϕX174 spike protein specified by cistron *G* which Air and Bridgen determined once Robertson *et al.* had begun the analysis of their fragment of ϕX174 DNA. Together these results unambiguously prove that the fragment of the ϕX174 genome which Robertson *et al.* have sequenced is the beginning of the *G* cistron.

This sequence, as Robertson *et al.* point out, has several striking features in common with the sequences of some of the ribosome binding sites of the RNA phages R17 and Qβ. As they say, "Thus a pattern of similarities seems to be emerging among known ribosome binding site sequences which may in the future be explained in terms of ribosome or factor specificity and thus play an important part in the control of initiation of protein synthesis". But if realization of the significance of these initiation site sequences is something for the future, the methods that Ziff and Robertson and their colleagues have pioneered can be immediately exploited to yield information about the base sequences of many DNAs, for they have the twin advantages of being direct and being generally applicable.
—From a Correspondent.

Climate and Ecological Change in East Africa

In 1962, Livingstone (*Nature*, **194**, 859) produced the first piece of direct evidence that 15,000 years ago the glaciers of Ruwenzori in East Africa were retreating at the same time as the Würm Glacier of Europe and the Wisconsin of America. Coetzee (*Nature*, **204**, 564 ; 1964) produced similar evidence for Mt Kenya, and Kendall (*Ecol. Monog.*, **39**, 121 ; 1969) has demonstrated climatic fluctuations in the Lake Victoria Basin. Large climatic changes in the comparatively recent past have clearly demonstrated that the vegetation and attendant faunal fluctuations must have been a marked phenomenon over most of the African continent. Indeed, it may well be that the Pleistocene overkill (Martin, *Nature*, **212**, 339 ; 1966) may be explained as much by climate as by human factors.

Climatic changes such as these may be considered to be recent in a geological sense, although in terms of present-day ecology they may be considered historic. If, however, the climate of the past hundred years in eastern Africa is examined, there is strong evidence to suggest that, superimposed on these longer term fluctuations, there are short-term changes that are of real significance to workers in the field of wildlife management today.

Western and Van Praet, on page 104 of this issue of *Nature*, convincingly demonstrate cyclical changes in both habitat and climate of the Masai Amboseli Game Reserve. The loss of fever trees (*Acacia xanthophloea*) from the basin has been noted over twenty years and especially during the past ten. The loss of this vegetation has been the cause of much concern, and Masai cattle and the elephant population have been blamed for the decline in tree density.

The whole Amboseli basin, which contained a large lake in the late Pleistocene, dried up during the Recent epoch. Western and Van Praet have found that the number of dead trees increases towards the basin centre and, because Masai cattle have been excluded since 1961, they conclude that domestic stock are not related to this tree death. Eighty-five per cent of the trees in the basin show damage from elephants, so that it might be presumed that they could be considered as being the primary cause of tree death. Seventeen per cent of the dead and dying trees are undamaged by elephants, however, so that Western and Van Praet looked for another primary factor, and demonstrate that increasing salination of the soil towards the basin coincides with high densities of dead trees. This increase in salination is associated with raised water levels and can be correlated in this closed drainage system to variations in rainfall.

Western and Van Praet show that Amboseli is sensitive to variations in water level which are indicated by alternation of hydrophytic and halophytic vegetation. Evidence from the oral history of Masai age sets clearly demonstrates that a halophytic vegetation covered the basin during the past century with a hydrophytic woodland forming in the first quarter of the present century and a strong reversal of this trend during the past ten years. These changes may well be shown to be the result of a long-term fluctuation in rainfall with a period of about 100 years. Thus in the closed drainage system of the Amboseli basin, and perhaps in similar areas such as Lake Manyara in East Africa, the primary cause of vegetation change seems to be rainfall, with elephants merely acting in a catalytic manner to accelerate changes already taking place.

Laws (*Oikos*, **21**, 1 ; 1970) has demonstrated that elephants act as important agents of change in many East African habitats especially in the conversion of woodland to grassland as has been observed in the Murchison National Park in Uganda and the Tsavo National Park in Kenya. In Tsavo these changes have been dramatic and a recent drought has led to the death of up to 5,000 animals. It has thus been suggested that the high elephant density and encroachment by man have been the primary causes for these changes. Although it is quite clear that the influence of man on the distribution of large mammals has been profound in many places, Western and Van Praet's article demonstrates the caution that must be used when interpreting vegetation changes in terms of man and animal numbers alone, for although to a large degree their influence is everywhere profound, the action of long- and short-term climatic changes may yet be shown to be a primary factor in the dynamics of these areas of variable and extreme climate.

The emergence of independent East African states with their rapidly expanding populations makes it imperative that the best possible economic use be made of the land. Vast tracts of these nations, however, fall into a semi-arid classification, so that such economic exploitation must of necessity be combined with a high degree of ecological planning and common sense. In recent years, the income that Kenya derives from tourism now heads their list of foreign earnings. This important fact clearly demonstrates that the sound management of game reserves, national parks and other amenity areas may well form the basis of future development and a sound economy.—M. C.

PROTEINS

In vitro, or Almost

from our Cell Biology Correspondent

The clawed toad, *Xenopus laevis*, has, of late, come to occupy a new ecological niche—the laboratories of molecular biologists many of whom, I suspect, have not since their boyhood days of jam jars full of frogs' spawn and tadpoles given amphibians a second thought. The reason for this sudden interest, from such an unexpected quarter, in *Xenopus* is that Gurdon and his school and collaborators have shown recently that globin messenger RNAs and calf lens crystalline messenger are, when injected into *Xenopus* oocytes, translated with fidelity and at a reasonable efficiency. In other words, *Xenopus* oocytes provide what almost amounts to a cellular cell-free system for studying the translation of at least some eukaryotic messengers, and in many laboratories any available mRNAs are being injected into these cells in the hope that they will be translated. It is hard to say what the failure rate is, but as Laskey, Gurdon and Crawford report in the current issue of the *Proceedings of the National Academy of Sciences* (**69**, 3665 ; 1972), the single-stranded RNA genome of encephalomyocarditis (EMC) virus, a picornavirus related to polio virus, can definitely be added to the list of successes.

After EMC RNA is injected into oocytes in the presence of 35S methionine, polypeptides not present in oocytes injected with saline are made. As polyacrylamide gel electrophoretic analysis reveals these newly made polypeptides have identical mobilities to the EMC proteins made when the virus replicates in ascites cells. The fact that tryptic fingerprints of three of the polypeptides made in oocytes are identical to the fingerprints of the co-electrophoresing EMC proteins made in ascites cells leaves no room to doubt that in oocytes EMC RNA is not only extensively but also faithfully translated.

That EMC RNA is translated in *Xenopus* oocytes is not particularly surprising, but it is interesting that in these cells, as in ascites cells, which support virus replication, the polypeptide product of translation is processed after translation. There is good evidence that EMC RNA, like polio virus RNA, is translated, during virus replication in mammalian cells, into a single large precursor polypeptide that is subsequently cleaved to yield the mature viral proteins. These mature proteins can be detected in extracts of oocytes injected with EMC RNA so that it must be assumed that they arise by specific cleavage of the primary product of translation. This obviously implies that oocytes contain proteases with specificities similar to those in mammalian cells and that mechanisms for the post-translational cleavage of polypeptides may be widespread among eukaryotic cells. Whether EMC can be persuaded to replicate in oocytes to yield infectious progeny virions remains to be seen.

Laskey *et al.* point out the advantages of the oocyte system over cell-free systems from ascites cells but the latter have their adherents and uses. Oberg and Shatkin (*ibid.*, 3589), for example, have used an ascites cell-free system programmed with EMC RNA to obtain further evidence for a unique initiation site for translation of this messenger. They fingerprinted the polypeptides made in the presence of 35S Met-tRNA$_M^{Met}$ and 35S Met-tRNA$_F^{Met}$; the latter tRNA translates only initiating AUG codons and fingerprints of polypeptides made in its presence reveal a single N terminal tryptic peptide containing 35S methionine. In other words, in this cell-free system, translation of EMC RNA and the RNAs of mouse Elberfeld virus and mengo virus is initiated at a unique site.

It remains true, of course, that compared with *Escherichia coli* cell-free systems for *in vitro* protein synthesis both ascites cell systems and the oocyte injection system are in their infancy, and one of the most remarkable results obtained of late with the *E. coli* system is that reported last April by Siegert *et al.* (*ibid.*, 888). They found that in such a system the RNA of avian myeloblastosis virus is translated faithfully to yield four of the group specific antigens of the avian RNA tumour viruses. Gielkens, Salden and Bloemendal (*FEBS Lett.*, **28**, 348 ; 1972) now report that RNA from Rauscher leukaemia virus and mouse mammary tumour virus stimulates polypeptide synthesis in an *E. coli* cell-free system. Furthermore, at least some of the smaller polypeptides which are made co-electrophorese with proteins of the respective virions, and polypeptides specified by the leukaemia virus are not related to those specified by the mammary tumour virus. By contrast, globin messenger and calf lens crystallin messenger stimulate very little protein synthesis and the short peptides which are made are the products of aberrant initiation.

Gielkens *et al.* also mention that in collaboration with Gurdon they have injected Rauscher leukaemia virus RNA into oocytes, but they failed to detect evidence of its translation. It seems therefore that for RNA tumour virologists the *E. coli* cell-free systems hold great and unexpected interest.

IMMUNOLOGY

Antigens and Ageing

from our Cell Physiology Correspondent

It is always interesting when results emanating from different laboratories are diametrically opposed to one another, but when such conflicting reports are published in the same journal the reader finds it hard to know what to believe. In a recent issue of *Experimental Cell Research* two groups report on their studies of the fate of HLA antigens in ageing diploid cells; one group comes to the conclusion that these change with age whereas the other group believes that there is no change.

The HLA antigens have long been recognized as being useful for distinguishing between the tissues of genetically different individuals and it is also known that diploid fibroblasts retain the HLA antigens of the individual from whom they were derived. This fact is often taken to be an indication of the normality or non-neoplastic nature of the cells, just as the fact that the cells can only be subcultured a limited number of times, after which degenerative changes are evident, is thought to be akin to what is understood as ageing.

Sasportes and his colleagues (*Nature*, **233**, 332 ; 1971) found that in some ten strains of fibroblasts obtained from skin biopsies, HLA antigens were lost as the cells grew older, the loss of antigens being evident before observable degenerative changes in the culture. Before this report appeared it had generally been accepted that histocompatibility antigens were retained throughout the life span of the cells, there being no change in the expression of HLA even during prolonged cultivation. Work

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Aminoacylation of Viral RNAs

One of the most intriguing features of the single-stranded RNA genomes of plant viruses such as turnip yellow mosaic virus (TYMV) and tobacco mosaic virus (TMV) is the occurrence at the 3′ end of these RNAs of the sequence . . pCpCpA. This same 3′ terminal sequence is common to all transfer RNAs and, like transfer RNA molecules, the RNAs of TYMV and TMV can be esterified by an amino-acid. TYMV can be specifically charged with valine and TMV can, as Litvak *et al.* report in next Wednesday's *Nature New Biology* (January 17), be specifically charged with histidine using yeast histidyl-tRNA synthetase to catalyse the reaction. Furthermore, Litvak *et al.* have found that both histidyl TMV RNA and valyl TYMV RNA can under appropriate conditions react with the protein synthesis elongation factor 1 (EF1) purified from wheat and with GTP to form a ternary complex of EF1.GTP.aminoacyl viral RNA. But TYMV RNA and TMV RNA that is not charged with an amino-acid does not react with EF1 and GTP.

Apparently the 3′ terminal sequence of these viral RNA genomes allows these RNA molecules to be acylated with an amino-acid and subsequently to form a ternary complex with an elongation factor. These events, as Litvak *et al.* speculate, may play a crucial part in regulating either the initiation of replication of these RNAs or the initiation of their translation by the protein synthesizing machinery of host plant cells ; for example, the complex of viral RNA with elongation factor may have a high affinity for ribosomes or, by analogy with the replication of phage Qβ RNA, elongation factor 1 may form part of a multimeric viral RNA replicase.

recently carried out in Hayflick's laboratory by Brautbar and his colleagues (*Exp. Cell Res.*, **75**, 31 ; 1972) supports the idea that there is no loss of HLA antigens in ageing diploid cells, for with cultures of WI38, WI26 and MRC-5 the same characteristic "tissue-type" was found even during the final senescent stages.

By contrast, Goldstein and Singal (*ibid.*, 278) report that in the strains of diploid fibroblasts which they have examined, loss of HLA antigens does occur and, as Sasportes found, this loss is detectable before the degeneration of a culture. In fact, it can even be used to diagnose the impending senescence of a culture.

The discrepancy between these various reports may have some purely technical explanation, the most likely one being that Brautbar and his colleagues examined only mass cultures of cells (Goldstein set out to look at cell clones rather than mass cultures). Indeed, because the mass cultures from which clones were derived showed no loss of HLA antigens it can be suggested that changes of antigen may be obscured when cells are grown *en masse*—probably as a result of the cooperation which is known to occur between cells in crowded conditions.

The method of assessing HLA may also have something to do with the discrepancy, for although Sasportes and Goldstein both used a dye exclusion method, Brautbar adopted a fluorochromatic one. Moreover, it is possible that the method of trypsinization may affect the result, for it is well known that the enzyme removes antigens from the surface of cells and it is therefore possible that the time at which HLA antigens are assessed after treatment is critical.

But can one interpret three negative reports and two positive ones in favour of the positive? The evidence which Goldstein provides with cell clones strongly suggests that one can, and it is interesting that with the different clones derived from a single cell strain the same HLA antigen is not always lost. Possibly this will support ideas which suppose that the molecular basis of ageing is of a random nature.

More important, however, is the fact that both Sasportes and Goldstein find that the loss of antigens is predominantly from the second of the HLA loci, the locus which is generally considered to be of greatest importance in so far as cell recognition is concerned. Might these results not therefore turn out to be a profoundly important link in what is known about ageing? If the loss of HLA antigens on these diploid fibroblasts reflects loss of antigens and surface membrane changes *in vivo* then it has important implications. Changes affecting either lymphoid or nonlymphoid cells would result in problems of self-recognition and loss of immunosurveillance so that autoimmune or neoplastic disease might follow.

True, it has yet to be established beyond any doubt that loss of HLA antigens or surface membrane changes do occur, but it is most attractive to interpret Sasportes's results and these recent results of Goldstein's in terms of immunological theories of ageing.

MEMBRANES

Lipophilia

from our Molecular Biology Correspondent

CURRENT beliefs about the state of proteins in membranes are encapsulated in artistic representations chiefly to be found in the pages of conference reports, in which they appear rather like marshmallows floating in a sea of treacle. The evidence is that, depending on the composition of the membrane, they can drift around with greater or lesser freedom, but that their orientation relative to the bilayer plane remains essentially invariant. There is, in other words, a large energy barrier to inhibit tumbling motion. There is also the possibility that the protein molecules attract around themselves a mantle of one or more of the phospholipid components of the bilayer, with which they associate relatively strongly. Practically nothing is known about the degree of specificity of protein-lipid interactions in membranes, or yet of their character and mechanism. There is scope for reasonable conjecture, not to say notions on the wilder fringes, involving such extravagant concepts as inside-out globular proteins.

One of the more conservative experimental approaches is to find a membrane enzyme which can be reversibly stripped of its lipids, and then use its activity after recombination with selected lipid components to assess the degree of specificity of its association with the bilayer constituents. In general the upshot has been that the requirements are only moderately specific. A very clear-cut and instructive new example of such a system comes from Garland and Cori (*Biochemistry*, **11**, 4712 ; 1972), working with the microsomal enzyme, glucose-6-phosphatase. The active preparations are lipoprotein particles, which lose their activity on treatment with phospholipases. These enzymes, however, are not nice to use in such a situation, on account of requirements for calcium ions or of the release of hydrolytic products, both of which complicate the interpretation in a disagreeable manner. What Garland and Cori have found is that under carefully defined conditions, non-ionic detergents, and in particular deoxycholate at sufficient concentration, permit reversible separation of the lipid. When the resulting mixture is applied to a 'Sepharose' column, the matrix of which excludes only very large particles, some of the protein, together with all the enzymatic activity, elutes in the void volume, but the bulk of the protein and nearly all the phospholipid are retarded, and emerge with different elution profiles. This protein fraction, almost free of lipid and inactive, can be completely reactivated by addition of new lipid. This only works, however, if some deoxycholate is kept in the mixture, or to

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Structural Probes and Peptides

IN next Wednesday's *Nature New Biology* (January 17) Beyer, Craig and Gibbons describe an extension of the application of fluorescent probes of protein structure to oligopeptides. The dyes, anilinonaphthalene sulphonic acid and *p*-toluidinylnapthalene sulphonic acid, are widely used as markers for local conformational changes in proteins. Their fluorescence is greatly enhanced when they bind on low-polarity sites, such as active-centre cavities, in the protein molecule. Using thin-film dialysis and fluorescence spectroscopy Beyer *et al.* studied the interaction of one of the dyes (TNS) with the cyclic antibiotic peptides, tyrocidines A, B, and C, gramicidin S–A, and bacitracin A. In thin-film dialysis the escape rate of a given molecule through a membrane is proportional to the concentration of that molecule on the inside.

With a membrane that passes free TNS much faster than the oligopeptides, Beyer *et al.* found that the escape of TNS is noticeably retarded by all the above peptides, as well as linear peptides, but not by succinyltyrocidine B. This indicates that coulombic interactions play a significant part in the binding process, for the effect of succinylation is to convert a positive charge, on an ornithine side chain, which would interact favourably with the sulphonyl group of the dye, into a negative charge.

In spite of the fact that there is interaction with the whole range of peptides, fluorescent enhancement was observed only in the presence of the tyrocidines. These are distinguished from the others by their tendency to self-association in aqueous solution. The associated form evidently provides an environment in which the TNS may be sequestered, so as to generate large quantum yields.

a lesser extent, if the phospholipids are first sonicated.

If, on the other hand, the bile salt concentration is too high, the activity falls catastrophically. Different phospholipids varied considerably in their ability to engender reactivation. The mono-unsaturated phosphatidylcholine is most effective, and generates full activity at half the concentration of total lipid present in the original preparation. The saturated version, dipalmitoylphosphatidylcholine, by contrast induces no activity whatever. The doubly unsaturated dioleyl derivative behaves similarly to the mono-unsaturated species. There is some precedent for this type of specificity relationship in regard to other membrane enzymes, but the mechanism is obscure. The role of the bile salt in promoting reactivation must be supposed to reside in its ability to destabilize the phospholipid micelles, and so make monomers available for reaction with the protein.

A different path towards the study of lipid-protein interactions has been pursued by Marchesi and his colleagues, who have been studying the red cell membrane glycoprotein (so-called glycophorin), which carries cell surface receptor groups. This molecule probably has a molecular weight of about 50,000, contains 60 per cent by weight of carbohydrate, and, so the story goes, is the most integral of membrane proteins, in that it projects right through the bilayer, whereas the bulk of red cell membrane proteins are to be found at the inner surface.

Segrest *et al.* (*Biochem. Biophys. Res. Commun.*, **49**, 964; 1972) have now sequenced a large tract of this molecule, which is evidently the very part that is normally lodged in the lipid interior of the bilayer. They have obtained cyanogen bromide and tryptic peptides with a good overlap. Two fragments are sialoglycopeptides, and therefore from the N-terminal end of the protein, which lies on the outer cell surface. Another is the C-terminal tract, which overlaps with a long tryptic peptide. Between them they define a sequence of fifty-one residues, all but the C-terminal end of which must be presumed normally to reside within the membrane bilayer. Twenty-three successive residues in the sequence are hydrophobic. At either end there is a considerable cluster of charged side chains, and it is reasonable to infer that these may be the parts of the protein that project into the aqueous media on the inside and outside of the cell. Segrest *et al.* refer to evidence of their own, as yet undivulged, that the hydrophobic stretch is an α-helix. Its length in this case would be some 35 Å, which is about right to span the bilayer. If the authors can confirm this model, it will clearly be a result of great interest.

LASSA VIRUS

A New Disease of Man?

from our Medical Virology Correspondent

THE name "arenovirus" defines a group of RNA viruses with a mean diameter of 110–130 nm, a dense well-defined envelope covered with projections and containing a variable number of electron-dense granules, giving a sandy appearance from which the generic name is derived (*Arenosus*, L. sandy). Other characteristics separate the arenoviruses from RNA lipid solvent-sensitive viruses. The group includes lymphocytic choriomeningitis virus, the Tacaribe complex viruses (haemorrhagic fever viruses of South America) and the recently described Lassa virus, all of which cross-react antigenically.

The dramatic story of Lassa fever began when two missionary nurses from Lassa, in north-east Nigeria, died in 1969 from a mysterious illness, and a third nurse, who was gravely ill, was flown to the United States. This nurse recovered and convalescent plasma from her was effective in the treatment of a laboratory worker, who acquired the infection while working with tissue cultures infected with blood from these patients (J. D. Frame *et al.*, *Amer. J. Trop. Med. Hyg.*, **19**, 670; 1970). The virus was isolated and characterized (S. M. Buckley and J. Casals, *ibid.*, 680) and Lassa fever was established as a new virus disease of man.

A further outbreak of Lassa fever, with a high mortality of 52 per cent among twenty-three patients admitted to hospital, was reported in Jos, Nigeria, in 1970 (H. A. White, *Trans. Roy. Soc. Trop. Med. Hyg.*, **66**, 390; 1972). Dr Jeannette M. Troup, who performed two autopsies while investigating Lassa

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Third Type of Pyroclastic Rock

PYROCLASTIC rocks—fragmental volcanic products ejected from volcanoes in explosive events—have usually been divided into two categories, fall deposits and flows. But in next Monday's *Nature Physical Science* (January 15) Sparks and Walker propose a third category, that of ground surge deposits. This category includes some deposits at present classified as pyroclastic flows—frothy, gas-filled glassy lava which bubbles from a volcanic vent during eruptions—and some deposits of *nuées ardentes*, which include the glowing avalanches that dominate the popular picture of volcanic eruptions.

The ground surge deposits are thus characterized by flows along the surface of the Earth, and are clearly distinguished from fall deposits, which show the effects of their passage through the air after ejection, for example in their internal stratification (see figure). But why is it necessary to distinguish between the new category and the pyroclastic flow category?

Active pyroclastic flows are believed to be fluidized by dissolved magmatic gas or by air trapped beneath the advancing flow. They travel as a dense mass, and pumice floats to the top of the flow, where it is preserved when the lava cools to form solid rock. These characteristics result in a structure which mantles the topography around the volcanic vent with a roughly uniform layer of rock.

Although ground surge deposits also mantle the topography, their thickness is not uniform—"they show a pinch and swell structure", as Sparks and Walker put it. Furthermore, they have an internal stratification which is not parallel to the bottom and top of the layer, and they extend out to only a few kilometres from the source. They are relatively thin—less than 1 m compared with the thickness of 10 m or more commonly associated with pyroclastic flows—and they can occur on relatively steep slopes (>10°) where pyroclastic flows do not solidify.

The overall picture painted by Sparks and Walker is one in which explosive volcanic activity produces, in addition to the ejecta thrown high into the air, both a dense flow, which chiefly follows the valleys, and a relatively low density ground surge, or "ash hurricane", akin to the ground surge generated in a nuclear explosion. The resulting thin ground surge deposit is very susceptible to erosion, and survives only when covered by other volcanic deposits; that explains why it has taken so long for the ground surge to be recognized as a separate category. Finally, the pinch and swell structure can be accounted for by a wave pattern, with wavelengths found so far in the region 4 m to 45 m.

Pyroclastic fall deposits. Dashed line is an erosional unconformity; the fall deposit above it shows internal stratification common among such deposits.

fever and who was primarily responsible for drawing attention to the condition, contracted the infection and died of it.

In March 1972 further cases of Lassa fever occurred among four patients and seven members of the staff in a hospital in the Zorzor district of Liberia in West Africa, and four died. The index case was a pregnant woman admitted to the obstetric ward, and all cases among the patients and members of the staff were in this ward. One of the fatal cases was an American missionary nurse who had direct contact with the blood of the index case (*Morbidity and Mortality Weekly Report*, **21**, 237 ; 1972). A more recent report (*ibid.*, 386) records a further sixty-four cases of Lassa fever admitted to hospital in Sierra Leone. Twenty-three (36 per cent) died, and the case fatality ratio among pregnant women was 75 per cent (six out of eight). One of the sixty-four cases was a nurse who pricked her finger on a needle used for obtaining blood from a patient who subsequently died of clinical Lassa fever.

This is the largest yet reported epidemic, and, unlike the previous outbreaks in Nigeria and Liberia, it consisted primarily of community-acquired infection. Evidence was obtained of family outbreaks of the fever in which spread has occurred among those with the most intimate contact. Man-to-man spread of Lassa virus undoubtedly takes place through contact with blood or infectious secretions, but a reservoir of infection has yet to be identified. Lassa virus is antigenically related to the rodent-associated haemorrhagic viruses of South America and to lymphocytic choriomeningitis virus, usually an inapparent infection of wild mice, but an animal source of Lassa virus or antibodies to this virus in wild rodents has not been found.

It is interesting that many features of this infection are reminiscent of the green monkey disease or Marburg virus infection (see *Nature*, **233**, 236 ; 1971), although, fortunately, no further cases of Marburg disease have been recorded since 1967. In the meantime, however, Lassa fever looms as an awesome new viral infection in tropical Africa, and the epidemiological propensities of this infection may be very wide with the modern means of fast air travel.

MINERAL RESOURCES

Boron from the Sea

from our Soviet Correspondent

NEW work on the sorption of boron compounds may provide a way of isolating the element from seawater. Although the concentration of boron in seawater is relatively low (8 to 9 g B_2O_3 m^{-3} in the Black Sea and 15 to 16 g B_2O_3 m^{-3} in the oceans), the estimated total content of boron in the seas and oceans (2.2×10^{13} tonnes B_2O_3) has provoked a considerable amount of research on the subject. New findings by Nikolaev of the Institute of Inorganic Chemistry of the Siberian Branch of the Soviet Academy of Sciences and Ryabinin of the Hydrophysical Marine Institute of the Ukrainian Academy of Sciences suggest a means of recovering boron, using ZrO_2 as a sorbent (*Dokl. Akad. Nauk SSSR*, **207**, 149 ; 1972).

Nikolaev and Ryabinin carried out a detailed survey of salinity, *p*H and temperature conditions affecting the sorption of boric oxide on various hydrated oxides, for different initial concentrations of the boron. Best results were obtained using hydrated zirconium oxide as sorbent and a *p*H value of 8 to 9—close to that of natural seawater. The effectiveness of the process was found to increase continuously with the amount of sorbent, practically total extraction of the boron (98 per cent) being obtained for a ratio of ZrO_2 to B_2O_3 of 400.

The experiments were performed with water from the Black Sea, and the good results obtained, even at these low concentrations, lead Nikolaev and Ryabinin to think that the use of a zirconium oxide sorbent may be an economically realistic method of recovering boron from the sea.

SEMICONDUCTORS

Transistor Revitalized

from a Correspondent

IT seems that the transistor, which only a few years ago was considered by many people to have reached the limit of its performance, is now a serious contender in the microwave region and may well extend its range to about 10 GHz. This was the theme of a timely symposium held at Imperial College, London, on December 13, and arranged by the Electronics Group of the Institute of Physics in collaboration with the Institute of Electrical Engineers.

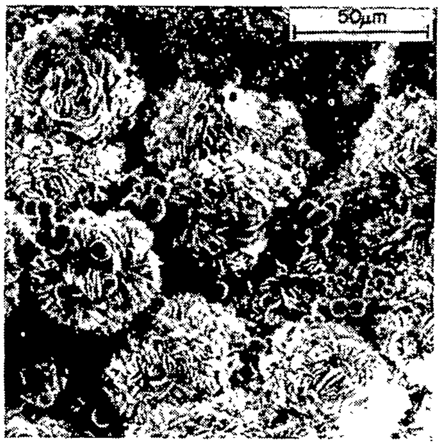
Many of the contributions reported significant advances in both silicon and gallium arsenide technology. In particular two speakers, D. J. Hinds (GEC Hirst Research Centre, Wembley) and Dr R. P. Arrowsmith (Post Office Research Department, Dollis Hill, London), discussed recent advances in the technology of silicon microwave bipolar transistors. It now seems that arsenic has replaced the more conventional phosphorus as the emitter dopant in npn devices. Improved cut-off frequency (f_T) and noise performance result in useful performance up to 4 GHz with promise of extending this to at least 8 GHz by reverting to an improved version of the old "mesa" design.

Many of the improvements can be attributed to great advances in optical photolithography, which mean that line

Laboratory-made Chert

THE flint-like rock called chert which has turned up in surprising quantities beneath the Atlantic to blunt the drilling bits of the Glomar Challenger research vessel continues to hold the attention of geologists. Last year Weaver and Wise of Florida State University reported that some of this chert, which is also found in other oceans, is composed of blades of cristobalite 300 Å to 500 Å thick gathered together in balls about 10 µm across (*Nature Physical Science*, **237**, 56 ; 1972).

These fascinating structures have now been reproduced in the laboratory. In an article in next Monday's *Nature Physical Science* (January 15), J. H. Oehler (University of California at Los Angeles) reports experiments in which aliquots of silica dispersed in water were subjected to temperatures of 150° C and pressures of 2 kbar for four weeks. The product, examined under the scanning electron microscope, consisted of 50–75 µm balls of platy, apparently hexagonal, crystals (see figure).



Oehler says that this hexagonal appearance of the artificial chert is characteristic of tridymite rather than cristobalite, which forms octahedral crystals, and he favours the view that what is being formed are hybrid crystals composed of layers of both tridymite and cristobalite, the tridymite structure dominating the morphology. X-ray diffraction data have so far been unable to confirm or deny the hypothesis. Oehler believes that this layered structure may well apply to the cristobalitic cherts recovered from the oceans.

widths for the emitter stripes in interdigitated structures of the order of 1 μm are now possible. To extend performance even further would require the use of electron beams to generate the mask patterns and possibly soft X-rays to project these patterns onto the semiconductor slice. New technologies such as ion implantation and proton-enhanced diffusion are being developed so that the doping profiles can be accurately controlled, for base widths as small as 0.1 μm are required.

R. C. Aubusson (Ferranti Ltd, Manchester) considered the use of polycrystalline silicon as an overlay for the emitter contact sites in order to introduce current sharing resistors to reduce the formation of hot spots and thus diminish the risk of thermal overload damage. Using this technique some 5 W at 2 GHz is now available. T. C. Denton (GEC Hirst Research Centre, Wembley) discussed the introduction of similar current sharing resistors into a mesh emitter silicon transistor, which allows pulse powers of the order of 150 W at 1 GHz to be obtained. Further advances in the gallium arsenide field effect transistor (FET) were described by J. A. Turner (Plessey, Allen Clark Research Centre, Caswell); changes in the structure from a one layer to a two layer epitaxial device have improved the mobility of the carriers in the active layer so that useful gain and noise performance up to 10 GHz is now available. Again the results are dependent on narrow gate widths of the order of 1 μm and further improvements depend on the smaller dimensions available from masks generated by electron beams.

Significant also was the extent to which computer simulation and new theories about the internal physics of the devices have been able to explain discrepanies between previous predictions and the actual performance of devices as reported by J. A. G. Slatter (Mullard Research Laboratories, Redhill). There has long been an unexplained difference between the predicted cut-off frequency (f_T) and current gain for bipolar silicon microwave devices, and a significant contribution from Dr H. De Man and R. Mertens (Laboratorium Voor Fysika En Elektronika Der Halfgeleiders, Leuven) showed that the phenomena can be explained by band tailing and formation of impurity bands. The effect produces a strong increase in the intrinsic carrier density in the emitter region and increases the charge storage of minority carriers, particularly in the emitter side wall of double diffused devices.

A further example of the use of computer simulation was given by J. C. Henderson, R. J. D. Scarbrough and Dr J. Earney (Post Office Research Department, Dollis Hill) who compared two identical bipolar transistor models, one in silicon and the other in gallium arsenide. Here was a case where predictions and comparisons could be based on the most recent advances in the two technologies. A plea was made that the recent gallium arsenide laser technology should be extended to the field of bipolar devices where even better performance is predicted.

Dr M. Merkel (Nuclear Research Centre, Grenoble) discussed the problems that arise when the more normal one-dimensional computer models are extended to cover the two-dimensional properties of practical devices. Many of the characteristics of FETs, for example, can only be adequately described in this way and can pose difficult problems if economical computer programs are to be devised.

One of the remaining problems that confront the designer of devices is that of the reduction of the package limitations that restrict the inherent frequency and power output of the active device. This was the theme of a contribution by J. R. Twistleton (GEC Hirst Research Centre, Wembley) who pointed out that the effect of parasitic reactances is particularly severe in microwave power devices because of their inherent low impedance.

EARTH STRAIN

Inland Tides

from our Geomagnetism Correspondent

THAT part of the Earth between Bradford and Halifax in the north of England is unlikely to be subject to accumulation of strain in the long term, but, as Bilham *et al.* (*Geophys. J.*, **29**, 473; 1972) have now discovered, the region is not free from short term nonlocal variations in strain. So much, at least, is clear from a survey involving 28 months of continuous strain recording. In July 1969, Bilham and his colleagues installed a prototype invar wire strainmeter in the disused Queensbury railway tunnel which lies in the north-east--south-west direction. As it soon became clear, the instrument possessed several deficiencies which prompted the development of an improved version. In the meantime, however, the prototype was kept in operation and proved to have a sufficiently high signal-to-noise ratio to record Earth tides clearly and thus to demonstrate the importance of tidal loading at a site well inland.

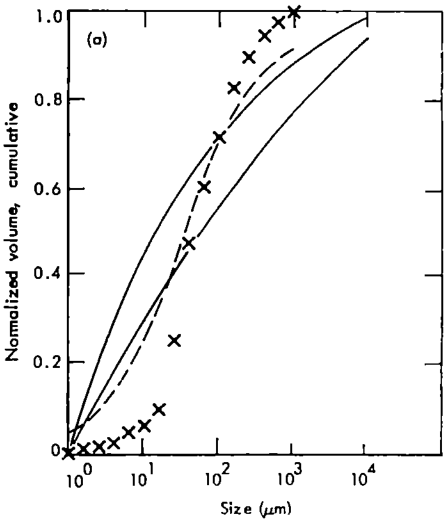
The strainmeter itself, fixed to the tunnel wall by expanding rock bolts, comprised a 10 m invar wire maintained under constant tension by gravity acting on a steel weight. Strain changes in the Earth produced a small rotation of the tension weight, representing

Surveyor Spacecraft Results Verified

ESTIMATES of the sizes of particles of lunar soil based on data relayed back to Earth by the Surveyor spacecraft, particularly Surveyor 3, have proved to be remarkably accurate. In next Monday's *Nature Physical Science* (January 15) Jaffe and Strand compare these calculations, made before lunar material was ever brought back from the Moon, with laboratory measurements of samples returned from the site of Surveyor 3 by the Apollo 12 astronauts (see diagram).

Methods used for the remote measurement of particle sizes included a measurement of the change in the photometric function of the surface when the soil was compressed by the spacecraft on landing. This led to the conclusion that the fine structure of the lunar material was smaller than 1 mm (which could just be resolved by the television cameras aboard Surveyor 3) and "larger than the order of 10 μm". Yet other estimates involved the laboratory simulation of the reproduction in the lunar soil of tiny ridges 50 to 70 μm high on the bottom of one of the footpads of Surveyor 3.

When the relevant data from all Surveyor spacecraft are taken into account, the agreement with laboratory measurements is quite close in the middle of the logarithmic range of particle sizes, but diverges somewhat at each end of the range. Jaffe and Strand conclude that their results augur well for the determination of soil sizes on other planets by means of automatic spacecraft landing there.



X, Laboratory measurements reported by Jaffe and Strand; ——, on-surface measurements (Surveyor 3); — — —, on-surface measurements (all Surveyors).

extension or contraction depending on the direction. Because of the orientation of the tunnel wall an extension actually represented a load bearing in the north-to-east or south-to-west directions, whereas a contraction represented loads in the north-west or south-east quadrants. A transducer was used to convert the rotation of the weight into a variable voltage suitable for chart recording. The problem of friction in the transducer and in the coupling of the transducer to the weight was one of the shortcomings of the simple instrument. A more serious problem was posed by the friction of the pivot linking the weight to the invar wire, although the effects of temperature and pressure in the wire proved less serious, because they turned out to be small by comparison with the effects of tides except at low frequencies.

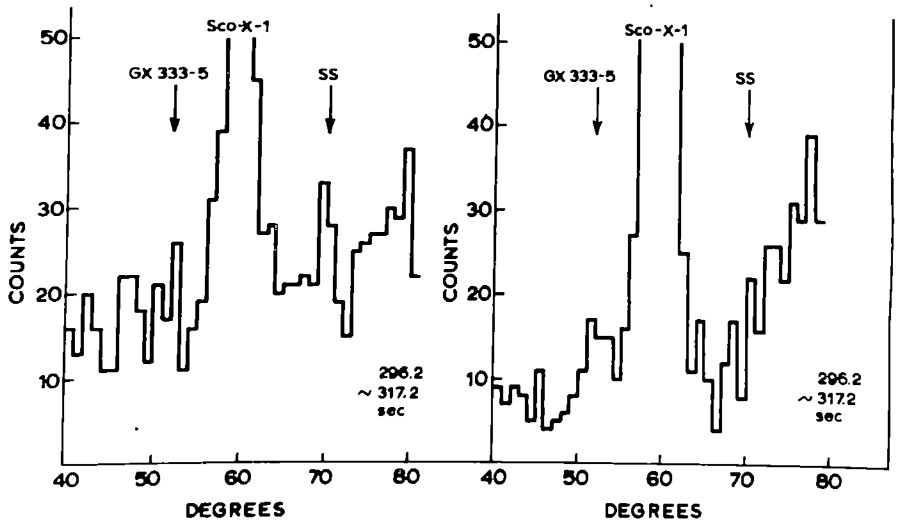
In spite of the problems, the recorded strain variations were of sufficient quality to warrant digitizing and spectral analysis. The chief interest of Bilham *et al.* was in the amplitudes of the various Earth tides and the degree to which the different components could be resolved, although they were also interested in studying the phase relationships between Earth tides as observed and calculated. To the latter end, therefore, it was necessary to determine Fourier components of the theoretical strain tide produced by the known motions of the Sun and Moon in a spherically symmetrical Earth having a distribution of elastic constants and density the same as that of the real Earth. This theoretical strain was calculated using the instantaneous tidal potential given by the positions of the Sun and Moon and the Love numbers calculated previously by Longman (*Geophys. J.*, **11**, 133 ; 1966). This allowed Bilham and his colleagues to generate a theoretical strain series over the same period as that over which a real strain was observed. Power spectra for both the observed and theoretical strain series were then determined, and all spectra were smoothed using a five-term Gaussian filter applied to the amplitude spectra.

The results showed that the smallest tides resolved (J and OO in G. H. Darwin's notation—*Scientific Papers*, **1**, 1 ; 1907) had strain amplitudes of 5×10^{-10} and that the frequency resolution was considerably better than Bilham and his colleagues had expected. The comparison between the observed and theoretical tides revealed the most striking difference in the properties of the diurnal and semidiurnal tides. The observed diurnal tides were roughly in phase with the theoretical tides, but had an amplitude lower by a factor of about three. The observed semidiurnal tides, on the other hand, agreed with the theoretical tides in amplitude but were about 180° out of phase. Such a difference in phase and amplitude could arise if the regional strain field were to be distorted by local inhomogeneities, although King (*Bull. Roy. Soc. New Zealand*, **9**, 239 ; 1971) concluded, on the basis of geological and rock mechanical evidence, that this should not happen at a site like Queensbury. Differences between observed and theoretical strains might also be observed if the fluid or solid Earth had some natural period of the order of 24 h or 12 h—but there are no such periods. Bilham and his colleagues are thus forced to the conclusion that the strain tides at Queensbury are strongly influenced by oceanic tidal loading.

This general conclusion is further supported by more detailed analysis. In simple terms, if the observed, theoretical and ocean load-induced strain signals are represented by functions of frequency—*H*, *G* and *L*, respectively—then *L* may be regarded as the difference between *H* and *G*, both of which are known. It is then possible to calculate the ratio of *L* and *G* (=*R*) which is clearly zero if there is no oceanic tidal loading at all. In fact, for semidiurnal tides, *R* ranges from 1.47 to 1.91 for the tidal peaks N, M_2, S_2 and K_2 (Darwin notation), thus clearly showing the dominance of the oceanic loading strains (*L*) over those produced by direct gravitational effects (*G*). For diurnal tides, *R* lies between 0.41 and 0.43, showing the oceanic loading effects to be smaller but far from zero. Some years ago, however, Cartwright (*Phil. Trans. Roy. Soc.*, **A263**, 1 ; 1968) analysed sea surface spectra for six tidal stations around the British Isles and also found that *R* is usually less than unity for diurnal tides.

The next step will clearly be to see if the implied oceanic tidal loading effects at Queensbury agree in detail with those predicted from real oceanic tides. So far this has not been done, but it is likely to be complicated because Queensbury will presumably be affected by tidal loading in both the North Sea and the Irish Sea and, to a lesser extent, in the North Atlantic. It is already clear, however, that strainmeters placed away from the coast can be used to investigate the regional behaviour of tides. And, as Bilham *et al.* point out, this could be of some social benefit, for inland strain stations could perhaps be used to detect tidal surges in the North Sea before they cause flooding.

Soft X-ray Source towards Galactic Centre



A ROCKET experiment flown on May 26, 1971, has led to the discovery of a discrete source of soft X-ray emission in a direction close to that of the galactic centre. In next Monday's *Nature Physical Science* (January 15) Bleeker and colleagues present spectra from several scans of the source and a best position error box. The source, designated SS, lies close to λSco, a bright spectroscopic binary of spectral type B1 V ; if SS is at the distance suggested for λSco by observations from OAO-2, then its luminosity in the band 0.37 to 1.9 keV is 2×10^{33} erg s^{-1}.

It is interesting that SS does not appear with any comparable brightness at hard X-ray frequencies. In the figure, the left-hand histogram is for a scan at 0.37 to 1.9 keV, and SS can be picked out readily ; on the right, the same scan at 1.9 to 6.5 keV, SS is completely absent, indicating that the source has a very soft spectrum.

Leukaemia Antigens and Immunity in Man

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Dr Harris describes recent research into the causes of leukaemia.

VIRUSES are associated with leukaemogenesis in both laboratory and outbred animals. In the laboratory mouse, susceptibility to several strains of virus leukaemia appears to be inherited and to involve an impaired immunological response to leukaemia specific antigens[1]. These animal models are intellectually satisfying, and it is tempting to extrapolate to human leukaemias. Indeed, the current interest in immunotherapy to some extent presupposes that putative human leukaemia antigens are capable of inducing an immune response. Although Mathé and his colleagues[2] claimed that remissions in acute lymphoblastic leukaemia had been maintained with immunotherapy, they could find little difference between the duration of remissions induced using Pasteur BCG alone, using injections of allogeneic leukaemia cells alone or a combination of both methods. The British "Concord" trial[3] using immunotherapy with modest doses of Glaxo BCG and without leukaemia cells failed to demonstrate any convincing advantage compared with maintenance chemotherapy. Others[4] have, however, claimed success with active immunization in leukaemia and results using irradiated allogeneic myeloblastic cells are encouraging[5]. Similarly, prolonged remissions in acute leukaemia seem to be "spontaneous" following chemotherapy[6] and might be due to the fortuitous development of effective immunity to leukaemia antigens.

In this article the usual abbreviations will be used—acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myelocytic leukaemia (CML) and chronic lymphatic leukaemia (CLL).

Leukaemia cells compete successfully with their normal equivalents as a result of poorly understood metabolic adaptations, and it is unlikely that human leukaemia results simply from immunological failure. Thus it has recently been demonstrated that primitive cells obtained from patients with AML can be induced to normal differentiation by soluble substances secreted by mature granulocytes[7,8] although it is possible that normal clones included with malignant cell suspensions are stimulated. These substances seem to be reduced in quantity in leukaemics[9] and this suggests that AML could be the result of a deficiency of a granulocyte "maturation factor" analogous to the colony stimulatory factor (CSF) described by Metcalf[10].

Metabolic alterations in leukaemic cells almost certainly involve alterations in cell membrane antigens, an idea which is supported by the suggestion in the hamster polyoma system that concanavalin A agglutination sites are related to malignancy and to the loss of cell contact inhibition[11]. Such membrane alterations, although incidentally antigenic, may be more important in indicating altered malignant cell growth leading to escape from effective control (Fig. 1). Remissions maintained with immunotherapy do not necessarily imply the existence of specific leukaemia antigens, and it is possible that the kinetic advantage enjoyed by leukaemia cells relative to normal leucocytes might be temporarily negated by intensive non-specific stimulation of normal leucocytes, perhaps associated with increased levels of CSF.

Two essentially different types of human leukaemia antigens may be postulated. The first type, involving qualitatively new antigens associated with virus infection (or genetic mutation), would be immunogenic and theoretically could be used for active immunotherapy. The second type, involving quantitative variations of normal antigens, would be less likely to be immunogenic. The definition of antigenic changes characteristic of leukaemia is therefore important for a variety of reasons. First, their immunogenicity and value in immunotherapy could be evaluated and the course of immunotherapy could be monitored with specific immunological tests permitting the assessment of the relative value of allogeneic and autochthonous leukaemic cells. It is vital to know whether the same antigens are found in different patients with the same form of leukaemia, and whether specific immunological tolerance is involved in leukaemia. Second, the characterization of leukaemia antigens might allow the identification of human leukaemia viruses not so far detected by electron microscopy; and third, irrespective of the immunogenicity of leukaemia cell membrane changes a study of these might assist an understanding of the nature of the metabolic and kinetic changes induced by oncogens.

Antibody Response to Leukaemia in Man

Antibodies reacting with leukaemia material have been reported in the serum of both leukaemia patients and normal individuals. For example, Seligmann *et al.*[12] detected precipitating antibodies in eight out of forty-five patients with acute leukaemia and granulopaenia. These antibodies gave strong

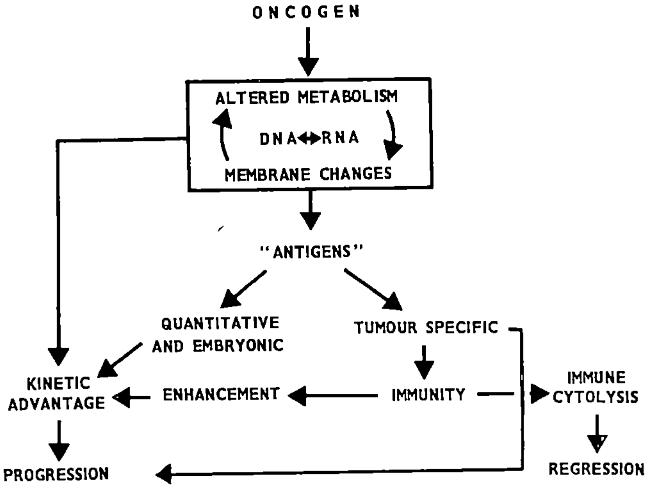

Fig. 1 Malignant transformation. Genetic changes following oncogenesis lead, it is suggested, to metabolic and membrane alterations which presumably confer kinetic advantages on malignant cells compared with their normal counterparts. "Tumour specific" antigens, but not quantitative variations in normal allo- and embryonic antigens, might be expected to lead to specific immunity and susceptibility to immune surveillance. Circumvention of the immune response might result from tolerance, antibody blockage or enhancement or non-specific immune depression.

reactions with ultrasonic lysates of both normal and CML leucocytes but not with CLL leucocytes. In a parous woman with acute monocytic leukaemia, Killmann[13] detected an autoantibody which, after absorption on autochthonous leukaemia cells and subsequent elution, reacted specifically with leukaemia cells. Garb *et al.*[14] claimed to have obtained indirect evidence for the presence of auto-antibodies in gel diffusion studies in CML (see below). Greenspan *et al.*[15], using passive cutaneous anaphylaxis in guinea-pigs and gel diffusion, found antibodies in the serum of most laboratory workers involved in human and animal leukaemia research. Greenspan also claimed to have induced similar antibodies by deliberate immunization of volunteers with human leukaemia brain material. Further studies using immunofluorescence suggested that the antigen responsible was located in the cytoplasm of leukaemia cells, and cross reactivity was reported between human and mouse leukaemia material. Using gel diffusion, immunoprecipitation and cytotoxic techniques, Carvalho[16] detected auto-antibodies in all five leukaemia patients that he tested (four ALL and one acute stem cell leukaemia). Similar antibodies were found in 92% of 180 normal people. The antigen used was a purified protein extract of a pool of cells from fifty leukaemia patients. Using complement fixation, Armstrong *et al.*[17] reported antibodies in 60% of healthy American adults when their serum was tested against lysates of leukaemia and of Burkitt's cell lines. Doré *et al.*[18] found evidence for auto-antibodies in patients with several different forms of leukaemia. Four different techniques (cytotoxicity, immunofluorescence, mixed cell agglutination and complement fixation) only yielded positive tests for twelve of fifty-one patients, and in most cases only one of the tests was positive. Yoshida and Imai[19], however, used immune adherence and studied untreated patients with various forms of acute and chronic leukaemia; they found auto-antibodies in fifteen out of thirty cases. Antibodies apparently increased in remission, and reactions with allogeneic leukaemic cells suggested the existence of at least two leukaemic specificities.

Cell Mediated Immune Response

Several attempts have been made to demonstrate cell mediated immunity to viable leukaemia blast cells obtained in the acute phase. Leukaemia cells can be inactivated after storage in liquid nitrogen and used in mixed leucocyte culture (MLC) with autologous remission lymphocytes, thereby avoiding allogeneic differences. In many cases remission lymphocytes undergo blastoid transformation and are stimulated to DNA production by inactivated autochthonous blast cells although the response varies from patient to patient[20-22]. Furthermore, after therapeutic injections of irradiated autochthonous or allogeneic leukaemia cells, the reactivity of suspensions of remission lymphocytes against active phase autochthonous blast cells appears to be increased[20,22], although the inclusion in cell cultures of autologous serum containing inhibitors (see below) and rebound following chemotherapy may lead to misleading results. The increased response was reported to be greater when autochthonous rather than allogeneic blasts were used to stimulate remission lymphocyte suspensions[22]. Leventhal *et al.*[23] also observed stimulation of remission lymphocytes by autochthonous blast cells and, in addition, reported *in vitro* cell mediated cytotoxicity against leukaemic cells and parallel cutaneous hypersensitivity to blast cell membrane. Such cutaneous hypersensitivity has been shown to correlate with remission[23,24]. Cytotoxicity was also studied by Rosenberg *et al.*[25], who incubated lymphocytes from apparently healthy relatives and from normal controls with lymphoid cells, labelled with isotopes, from leukaemia patients and their normal identical twins. In four of six families studied, lymphocytes from family members were cytotoxic for lymphoid cells from a patient, but not from the identical twin.

These studies[20-23,25] suggest that leukaemia cells have surface antigen determinants to which immunological reactivity exists and which can be increased by immunotherapy. Rudolph *et al.*[26] failed, however, to find evidence for leukaemia associated antigens using mixed leucocyte cultures and testing four sets of identical siblings where one member of the set had acute leukaemia in relapse. In no instance did the leukaemia cells of the patient stimulate the lymphocytes of the normal twin. By contrast Bach *et al.*[27] investigated siblings, who, although not identical twins, were HL-A identical, and detected unidirectional stimulation which they interpreted as evidence for leukaemia associated antigens. The failure of Rudolph to detect stimulation in MLC might be ascribed to the lack of immunization in the normal twin, but it is then difficult to understand why Bach detected a mixed lymphocyte response in rather similar circumstances unless other non-HL-A antigens contribute to the mixed lymphocyte response between non-identical siblings.

Knight *et al.*[28] claim that established cell lines stimulate both allogeneic and autologous lymphocytes in culture, whether the cell lines are established from normal or leukaemia material, and they suggested that established cell lines develop membrane antigens not found on autologous normal lymphocytes. It was implied that the response of lymphocytes to autochthonous leukaemia cells was due to similar surface antigens and not necessarily to leukaemia specific antigens. The presence of "new" antigens on cell lines, however, in no way invalidates the evidence that leukaemia blast cells have specific antigens. The results of Knight and her colleagues emphasize the importance of the putative cell membrane changes which accompany altered cell kinetics—in this case those changes involved in adaptation to the abnormal condition of established culture.

In summary, the existence of leukaemia antigens in man has been suggested by immune reactions to autochthonous and allogeneic leukaemia material using a variety of techniques. These include the detection of antibodies by immunoprecipitation, leucoagglutination and mixed cell agglutination, immunofluorescence, serological cytotoxicity, complement fixation and passive cutaneous anaphylaxis in guinea-pigs. Cell mediated immunity has been detected by lymphocyte stimulation (MLC) and cytotoxicity *in vitro* and by cutaneous hypersensitivity against leukaemia material. It is not known whether the various forms of immunity that have been demonstrated inhibit or enhance the evolution of leukaemia. The variations in the strength and frequency of the immune reactions observed probably result from the different test systems and antigenic preparations used and the heterogeneity of the clinical types and stages of leukaemias involved. Two aspects of most studies are particularly poorly defined. The first involves the identification of leukaemia antigens. The second, which will be considered later, concerns possible variations in the level of general immune responsiveness at various stages in leukaemia.

Characterization of Leukaemia-associated Antigens

There have been many attempts, using xenogeneic antisera, to define specific antigens in leukaemia, although antigens defined in this way are not necessarily those that might provoke auto-immunity. Seligmann[29] claimed to have demonstrated antigens characteristic of CML in acute crisis. He immunized rabbits with whole human leukaemia cells and, in tube and gel immunoprecipitation, tested the resulting antisera against extracts of leukaemia leucocytes and serum from leukaemia patients. One antigen, apparently an α globulin, was found in the serum of both normal and leukaemia patients but, in acute relapse, a number of additional antigens appeared in the serum of patients with CML. Carvalho[30] employed rabbit antisera and purified fluoro-carbon extracts of protein from human leukaemia cells; he found extra precipitation lines with leukaemia material and noted that these antigens were different in CLL and acute stem cell leukaemia.

Korngold *et al.*[31,32] studied the insoluble sediment from homogenized normal and leukaemia leucocytes with rabbit antisera and gel diffusion. They found that normal cells and CML leucocytes, by contrast with CLL, were good immunogens. They claimed to have defined three classes of antigens: antigens 1 and 2 ("granulocyte antigens") were found in normal leucocytes, in CML and in leucocytes from patients with leukaemoid reactions. Antigen 1 was reduced or absent in blast cells, which by contrast contained antigen number 3, which was also found in normal spleen and liver material. Antigens 1, 2 and 3 were absent from some acute leukaemic, from CLL cells and from two established leucocyte lines.

Garb *et al.*[14], using rabbits rendered partially tolerant to normal antigens, raised antisera to whole blood from human leukaemia patients. In gel diffusion studies they detected antigens in AML which were not found in normal buffy coat. Antisera raised against CML blood reacted with both AML and CML but not with normal buffy coat material. CML leucocytes did not, however, react in gel diffusion with rabbit antisera, and Garb suggested that this was due to auto-antibodies coating CML cells. Also using antisera raised in rabbits rendered partially tolerant to normal human antigens, Hyde *et al.*[33] claimed to have detected antigens common to AML and CML and not found in normal leucocytes or in cells obtained from patients with CLL.

Yata *et al.*[34], using rabbit antisera raised against homogenates of lymph node cells from a patient with acute lymphoblastic leukaemia, detected cross reactivity in gel diffusion studies with most leukaemias, lymphomas and with some spleens and lymph nodes from normal individuals. Thymic cells obtained from normal individuals and foetuses (3 months gestation and later) were also positive. Yata believed that the antigen detected was similar to that of Tallberg *et al.*[35], and may represent a human thymus antigen comparable to mouse TL. Yata suggested that the thymic antigen on myelogenous leukaemia cells might be acquired during the passage of these cells through the thymus.

Mann *et al.*[36] prepared antisera by immunizing rabbits with purified cell membrane components from a tissue culture cell line, Raji (derived from a patient with Burkitt lymphoma). These sera, which were not absorbed before use, were found to be cytotoxic to peripheral white blood cells from some patients who had ALL or AML in relapse and not to cells from normal unrelated individuals. Evidence was, however, obtained which suggested that the antigenic determinants were present on white blood cells from some apparently normal relatives of leukaemia patients and from all the long term lymphoid tissue culture cell lines that were tested but not PHA transformed lymphocytes.

We have prepared solubilized partially purified extracts from haematologically defined human leukaemias[37–39]. The methods used were derived from those employed by Davies *et al.*[40] to extract membrane antigens from normal human spleens. Antisera raised in rabbits against these leukaemia materials react in gel diffusion and cross-over electrophoresis with both normal and leukaemia material. If, however, these antisera are absorbed with normal human serum and with extracts of normal spleens, reactivity with the normal material is greatly reduced. Absorbed antisera retain the ability to precipitate both leukaemia extracts and similar extracts made from normal embryos. Antisera prepared against material from patients with AML give strong precipitation lines with the serum of patients with AML or CML, but only occasional weak reactions with serum from patients with CLL or ALL and from normal individuals.

Problems and Pitfalls in Characterization

There are many variables in reported studies of leukaemia antigens. In some reports the haematological type and stage of leukaemia are not made clear. The methods for extracting antigens for immunization vary greatly, and a clear distinction is not always made between water soluble and water insoluble fractions. In these circumstances considerable difficulty will be encountered as water soluble fractions of granulocytes strongly precipitate with extracts of other cells or with dialysed normal human serum[31]. Antisera produced against a mixture of antigens may contain antibodies with different optimal zones of reactivity, and one antigen may form a precipitation line whereas for another the ratio of antigen and antibody concentrations is unsuitable. Antigens which are good immunogens when injected into animals are not necessarily the most important antigens in distinguishing between different cell types.

Cross reactions between normal leucocytes and CML cells are reported in many studies, and are of unknown significance. Antisera raised against leucocytes contaminated with serum will react with plasma proteins in gel diffusion. Even when well washed leucocytes are used and antisera are absorbed with normal human serum, problems may arise because there is a wide range of human specific antigens against which rabbit antisera may inadvertently be raised[41]. Determining the correct method for absorbing unwanted specificities is often laborious and minor technical variations may produce anomalous results. Abnormal serum proteins which are not leukaemia specific may also cause difficulties in interpretation. For example, C-reactive protein (presumably the result of tissue breakdown) is found in the serum of over half the patients with acute leukaemia and can be demonstrated easily by gel diffusion studies[42]. Similarly a foeto-protein (α2H) found in large quantity in foetal liver appears in the serum of patients with many different blood diseases including leukaemia[43]. The distinction between such non-specific antigens as C-reactive protein and α2H, on the one hand, and "true" tumour antigens is, however, blurred, for it is known that carcino-embryonic antigens[44] and α1 foeto-protein[45], previously thought to be pathogenic for particular malignancies, are present in minute quantities in normal individuals (see later).

Variations in Normal Iso-antigens

Several variations in leucocyte allo-antigens have been described in leukaemia. For example, Kassulke *et al.*[46], using mixed agglutination, claimed that there occurs in some acute leukaemias a reduction in group A and H antigenic specificity together with the appearance of the same M and N antigens which are found on the patient's red cells. These authors stated that M and N antigens are not normally demonstrable on leucocytes, and account for the reduction in A and H activity by the acquisition by leukaemia cells of neuraminic acid with M and N specificity.

Variations in HL-A antigen expression in leukaemia have also been reported. Pegrum *et al.*[47] claimed that leukaemia cells may acquire new HL-A antigens. "Additional" HL-A antigens have been observed in lymphoid cells in culture[48,49]. We have suggested[50] that anomalous HL-A typing results on occasions from the contamination of HL-A antisera with antibodies too weak to be detected by cytotoxic tests employing normal cells. For example, low titre EB virus antibodies are detectable in almost 50% of normal individuals[51]. We find that AML blasts in common with established cell lines are more sensitive to HL-A antisera. Although shorter incubation times and a lower concentration of rabbit complement may yield clear results, some HL-A antisera continue to give anomalous results with leukaemic cells suggesting that they contain antibodies directed against antigenic determinants not demonstrable on normal lymphocytes.

Goret *et al.*[52] claimed that lymphocytes from patients with acute leukaemia were lysed by a wide range of xenogeneic and allogeneic antisera in circumstances in which normal lymphocytes are not, and that the lymphocyte cell membrane in leukaemia is abnormally fragile. In a small series of children with ALL we have not detected increased lymphocyte sensitivity to cytolysis by HL-A antisera (Harris, R., and Wentzel, J., unpublished observations). Schlesinger and Amos[53] believed that leukaemic cells were generally more reactive than normal cells with allo-antisera.

It is interesting to contrast the apparent gain of HL-A antigens with the phenomenon of antigenic modulation in mice[54,55]. TL ("thymus leukaemia") antigens are normally present on thymic cells in "TL positive" strains of mice, and may appear in the peripheral blood when TL positive or TL negative mice develop leukaemia. The appearance of TL on blood cells is associated with a quantitative diminution of normal H-2 histocompatibility antigens. If TL positive cells are injected into specifically immunized TL negative mice[54] or incubated with non-cytotoxic TL antisera *in vitro*[55], TL antigenicity decreases and H-2 antigenicity increases. Antigenic modulation thus involves a reciprocal relationship between H-2 and TL. Although no equivalent phenomenon has so far been discovered in human leukaemia, Martin *et al.*[56] have reported that a normal antigen diminishes in quantity in parallel with the increase in carcino-embryonic antigen in colonic tumours. Quantitative reduction in the expression of normal antigens may be a rather common phenomenon accompanying tumour antigens and human leukaemia cells should be re-examined with more discriminating techniques, and making allowance for possible membrane fragility, to detect a reduction in the expression of HL-A antigens.

Quantitative antigen changes may also result from alterations in the proportions of different circulating leucocyte types. In CLL, for example, cells tentatively identified by immunofluorescence as "B" cells make up more than 85% of the peripheral blood lymphocyte population compared with 34% in normal individuals[57]. These studies show that an increase in total immunoglobulin receptors occurs due to an increased number of "B" cells rather than an increased density of immunoglobulin receptors on the cell membrane. Very little is known about the spatial distribution of antigens on the surface of human leukaemia cells. Using the phenomenon of steric interference Legrand and Dausset[58] have, however, begun to map the position of HL-A antigens on normal lymphocytes, and Aoki and his colleagues[59] studying mouse cells have demonstrated the existence of an antigenic "grid" in which a number of antigens characteristic of thymus derived lymphocytes exist in a definite spatial relationship with each other. Although these observations have been criticized by Davis *et al.*[60], it is reasonable to hope that a study of human leukaemia cells will clarify some of the changes which are suspected to occur provided leukaemia associated antigens can be accurately defined and effectively monospecific antisera to these antigens raised.

Embryonic Antigens

Our results[39] indicate that cross reactions occur between solubilized partially purified extracts of leukaemia cell membranes and extracts prepared in a similar way from normal human embryos of about 12 weeks gestation. A limited number of experiments suggest that the antigens concerned is not α1F. α2H occurred in more than half of the patients with AML, but could be distinguished from other antigens of solubilized leukaemia cell membranes. In studies in collaboration with Professor Berg of Oslo we compared an anti-AML serum with rabbit antiserum, raised against human amniotic fluid, which did not react with α2H. These antisera gave reactions of identity in immunoprecipitation and very similar reaction patterns ($P < 0.001$) with a panel of sera from patients with leukaemia. Others[61] have also found evidence for the existence of embryonic antigens in human leukaemia material.

The reappearance in cancer of antigens characteristic of the foetus is now known to occur in many different human and animal tumours[62]. This has been variously ascribed to the specific derepression of genes important in embryonic development (perhaps indicating a reversion to an uncontrolled embryonic pattern of cell growth), to the persistence of small numbers of "embryonic cells" or to stem cells in adult tissues and to a general disruption of normal gene control (perhaps associated with chromosomal aneuploidy) allowing the random expression of many genes normally repressed in adult cells.

Embryonic antigens, notably α1F and CEA, have been shown to occur in nanogram quantities in normal adult tissues and plasma[44,45], and it is not clear to what extent these antigens might be auto-immunogenic in cancer patients. This is a very important question because *a priori* specific immunotherapy would be more likely to succeed if qualitatively new (tumour specific) antigens are involved. Nanogram quantities of embryonic antigens in normal adult serum may, however, not be sufficient to maintain tolerance, for recent work[63] with immunoglobulin idiotypes suggests that an immune response can be mounted against antigens previously present in subtolerogenic concentrations.

Surface Charge

It is believed that the affinity of antibodies for cellular immunogens is governed by an inverse relationship between the relative net electrical charges[64], and Ambrose[65] has suggested that cancer cells have increased surface negativity. Sahasrabudhe *et al.*[66] claimed to have produced antibodies "specific" for leukaemic cells by immunizing rabbits with normal leucocytes which were previously tagged with 1-fluoro-2-4-dinitrobenzene (FDNB). They ascribe this phenomenon to alterations in net surface charge induced by FDNB. Others, however, have not found differences in surface charge in unmodified ALL cells[67].

Association between HL-A and ALL

Walford[68] reported a significant excess of HL-A2 and HL-A12 antigens in children with ALL, and suggested an analogy with Gross virus induced mouse leukaemias where inbred strains of H-2^{kk} genotype are susceptible to specific oncogenic virus whereas H-2^{dd} mice are resistant. Mice which develop leukaemia due to Gross virus may lack a "resistance gene" (Rgv-1) located within the H-2 chromosomal region[1]. The demonstration of comparable associations between susceptibility to leukaemia and histocompatibility type in man would provide important evidence favouring the similarity between murine and human leukaemia and strengthening the hypothesis that human genetic susceptibility to oncogenic viruses is involved. By analogy with experimental animals, particularly the mouse, the HL-A chromosomal region may contain genes controlling susceptibility to leukaemia and other diseases and the levels of specific and general immune response to various antigens (reviewed by McDevitt and Bodmer[1] and Walford *et al.*[69]). Susceptibility to leukaemia may be determined by recessive mutant genes governing a poor immune response to leukaemia (virus) antigens. Alternatively, the antigenic products of co-dominant genes in the HL-A chromosomal region may be so similar to leukaemia or virus antigens that individuals positive for such antigens may be unable to produce an immunological response to them. Unfortunately the genetic heterogeneity of human populations makes the search for associations between genetic markers and diseases extremely difficult[70].

Viruses and Leukaemia

It is likely that at least some human leukaemias will be shown to be associated with oncogenic virus, although it would be inappropriate to attempt to detail the evidence here. Virus particles have not been found consistently in leukaemia in man[71], but the antigens of tumours and leukaemias in animals have been reviewed[72] as has the evidence for the involvement of viruses in human cancer[73]. RNA viruses seem to manufacture DNA in mammalian cells by means of reverse transcriptase, and it has been suggested that such DNA may be incorporated into the mammalian genome and transmitted in the germ line[74]. Work with feline viruses[75] has provided a model in which RNA oncogenic virus is probably transmitted vertically and horizontally in outbred animal populations overcoming the objections frequently raised against the relevance of leukaemia of inbred mice. Cat leukaemia virus, like other C-type RNA viruses, can be characterized by type and group specific antigens using allogeneic and xenogeneic antisera. Interspecies antigens, which appear to be common to virus leukaemias affecting cats, rats, mice and hamsters, may, however, prove to be more valuable in the search for leukaemia viruses in man.

Spiegelman has shown that RNA from Rauscher mouse virus leukaemia can be used succesfully to detect homologous nucleoprotein in human leukaemia^{76}. Furthermore, his group has demonstrated complexes of 70S RNA and reverse transcriptase in the white blood cells of 95% of leukaemic patients examined. DNA synthesized by these complexes hybridized to the RNA of Rauscher leukaemia virus but not to other animal tumour viruses studied. Such complexes were found in patients with ALL, AML and CML^{77}.

Depression of the Immune Response in Leukaemia

I have suggested in this article that there is evidence, albeit fragmentary, for specific antigens in human leukaemia. Why is the immune response to these antigens apparently ineffective? A general depression of immunity has not been conclusively demonstrated in untreated acute leukaemia$^{78-84}$. Much attention has, however, been concentrated on the *in vitro* lymphocyte response to phytohaemagglutinin (PHA) in an attempt to overcome the variables inevitably associated with the evaluation of immunity. Most studies have shown that the PHA response is relatively normal in patients with untreated acute leukaemia, and although some believe that the response is depressed by chemotherapy it recovers rapidly when treatment is stopped. The dose of PHA used in many studies is, however, much in excess of that which gives the most sensitive discrimination between normal and abnormal responses^{85,86}. We have found^{87} that the response of lymphocytes from normals or leukaemics to low (7 μg ml.$^{-1}$) doses of PHA is often greatly reduced in the presence of serum obtained from patients with untreated AML and ALL (Fig. 2). We attribute this to the presence of inhibitory factors in the serum of leukaemics only occasionally attributable to complement dependent cytotoxic HL-A antibodies.

Hersey *et al.*^{88} detected blocking factors to antibody dependent *in vitro* killing of leukaemic blast cells by lymphocytes. In one patient of the small series studied so far relapse was preceded by the appearance of "blocking factors" and with the appearance of our inhibitory factors. The *in vivo* importance of antibody dependent lymphocyte killing of leukaemic cells and the role of blocking factors are currently being assessed. It may eventually become clear that the Hellström model^{89} of antibodies blocking cytotoxic lymphocyte activity against tumour cells is also valid for leukaemia.

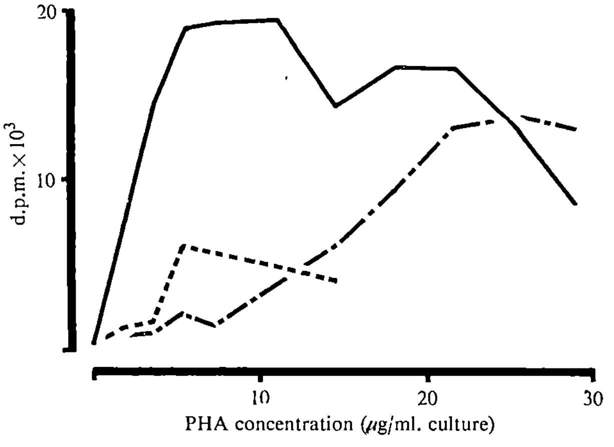

Fig. 2 Inhibitory effect of leukaemic serum on ^{125}I udr uptake by PHA stimulated lymphocytes from a normal donor. ——, Normal autologous serum; — — — — —, serum from untreated ALL; - - - -, serum from untreated AML.

Serum inhibitors of the lymphocyte response occur in many different diseases^{90}, although their immunological significance is unknown. Field and Caspary^{91}, using washed lymphocytes, claimed, however, a normal *in vitro* response to PPD in patients with sarcoidosis, although the Mantoux test was negative and the addition of a 1 in 60 dilution of autologous serum abolished the *in vitro* response to PPD. Our results demonstrated that leukaemia sera frequently inhibit two-way mixed normal lymphocyte reaction as well as the PHA response. This suggested that serum inhibitors have *in vivo* immunological significance and perhaps interfere with the function of otherwise normal lymphocytes. Serum factors may also inhibit normal haematopoiesis and consequently alter the kinetic balance between leukaemia and normal cells (Lajtha, personal communication).

Immune Phenomena

The current preoccupation with immunotherapy is based on the assumption that potentially immunogenic changes occur during leukaemogenesis. Many antigen alterations in leukaemia are, however, not necessarily immunogenic; for example, an increase of embryonic or normal allo-antigens and the vertical transmission of a leukaemia agent may be associated with immunological tolerance. Nevertheless the intellectual appeal of immune surveillance is so great that one is almost compelled to believe that immune phenomena are involved in leukaemia and a review of the literature indeed suggests that potentially immunogenic antigenic changes characteristic of human leukaemia occur. Thus auto-antibodies have been reported at various stages in the evolution of leukaemia, antibodies to leukaemia cells have been described in the serum of normal individuals who have been in contact with human or animal leukaemia and peripheral lymphocytes respond *in vitro* to autochthonous leukaemia cells in a way that suggests that immunogenic leukaemia associated antigens are present. If auto-immunogenic leukaemia associated antigens exist, it must be supposed that the results of immune response are ineffective in established leukaemia.

The serum of patients with untreated acute leukaemia is frequently inhibitory to lymphocytes both in the PHA and the mixed lymphocyte responses. These factors inhibit allogeneic and autochthonous lymphocytes from leukaemia patients and normal individuals alike. Some inhibitors may be α globulins^{92}, and we have observed a marked fall in both inhibitors and α2H levels following the induction of remission in AML (unpublished observations). It is not clear whether the presence of inhibitors is merely incidental or whether they play an important part in suppressing normal immunity and haemopoiesis.

Under the aegis of the MRC a trial of immunotherapy in AML is now in progress. This trial includes a programme of investigations designed to study both specific and non-specific immunological responses. An important object of the trial will be to evaluate the relationship between the afferent (recognition) and efferent (cytotoxic) arms of immune responsiveness in leukaemia and to study the effects of immune depression, whether endogenous or due to chemotherapy, on putative leukaemia specific responses.

There is almost certainly no single cause for leukaemia, and individual susceptibility is probably governed by a complex interaction of oncogen and inherited host resistance. The concept of immune surveillance does not require that immunity should have a primary role in the inception of cancer and the fundamental change is the imperfectly understood metabolic adaptations of malignant cells which allow them to compete successfully with their normal counterparts. There is, however, evidence for auto-immunogenic antigens associated with human leukaemia, and it will probably be shown that in some cases these result from infection with oncogenic virus. A knowledge of such antigens would allow an aetiological classification of human leukaemia and would provide a rational basis for successful immunotherapy following cyto-reductive chemotherapy.

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Premonitory Changes in Seismic Velocities and Prediction of Earthquakes

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Large premonitory changes in ratio of seismic P and S velocities correlate with time of occurrence and size of earthquakes at Blue Mountain Lake, New York. These changes may be related to the opening of cracks or to changes in pore pressure.

WE report here large changes in the ratio of compressional to shear wave velocities (v_p/v_s) in the source region of several small to moderate size earthquakes in the eastern United States. Although our results are only preliminary and many additional data remain to be analysed, the changes we observe are pronounced and are similar to observations reported for the Garm region of Central Asia[1,2]. To our knowledge this is the first time that the work in Garm has been repeated successfully elsewhere. We hope these preliminary observations will encourage the search for similar phenomena premonitory to earthquakes in other areas.

A series of small to moderate size earthquakes, the largest of which was magnitude 3.6, in the Adirondack region of northern New York State (Fig. 1) in 1971 provided an unusual opportunity to install a network of portable seismographs within a few kilometres of the source region[3]. Because the focal depths of the events in this swarm were between 0 and 3.5 km, a large percentage of the seismic ray paths were within the volume defined by the spatial distribution of the shocks in the swarm.

Much of this report seeks to document that large and significant changes in the P to S velocity ratio do, in fact, occur and that this ratio decreases prior to the larger shocks that we studied. This decrease, which is up to 13%, is similar to premonitory changes before magnitude 4 to 5 earthquakes in Central Asia. The time duration (but not the size) of the anomalous decrease in velocity ratio is longer the larger the magnitude of the earthquake. Although we do not understand the causal mechanism for these large changes in velocity ratio, we discuss several factors such as changes in pore pressure, crack development and creep that may cause these large anomalies in velocity ratio. Detailed monitoring of the velocity ratio and an understanding of the causes of these changes may provide sound bases for predicting earthquakes in general or for ascertaining the type of earthquake or seismic area for which this technique is applicable.

Description of Swarm

Six portable high-gain, high-frequency seismographs were installed (Fig. 1) near Blue Mountain Lake (BML) a few days after two events of magnitude 3.6 and 3.4 which occurred on May 23, 1971. Observations of the swarm, which consisted of thousands of recorded microearthquakes, continued for several months. Events as large as magnitude 3.3 were recorded by the portable network. We report here the velocity ratio determined from small events before and after the July 10 and 27 events of magnitude 3.3 and 2.5.

Sbar *et al.*[3] analysed the spatial distribution of events in the swarm and report a composite focal mechanism involving thrust faulting. The earthquake foci are confined to a tabular zone that dips gently eastward from the surface to a depth of about 2 km and then steepens for depths from 2 to 3.5 km. The surface projection of this zone is about 2 km on a side and is somewhat larger than that involved in the foreshocks and aftershocks of the July 27 event of magnitude 2.5 (Fig. 1).

v_p/v_s Technique

For each of several hundred small earthquakes the arrival times of P and S waves at each seismograph station were read with a precision of 0.01 s using a microscope. Onsets of both the P and S waves were very impulsive; problems of phase identification were negligible for the events reported here. S-P times for each shock were plotted as a function of P arrival times as illustrated in Fig. 2 for three earthquakes. The slope of these curves is the ratio of the travel time of S waves to that of P minus one. For a homogeneous material the slope is v_p/v_s-1. The precise fit of the data points in Fig. 2 to straight lines attests to the accuracy of the readings of arrival times and to the homogeneity of the medium. One factor responsible for the small scatter of the observations

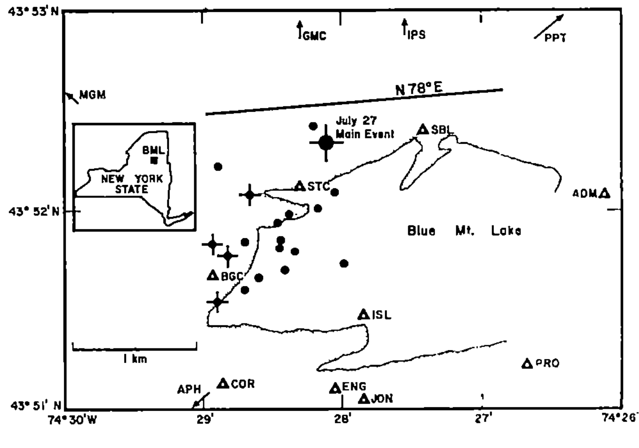

Fig. 1 Location of Blue Mountain Lake (BML) earthquake swarm. Solid circles are epicentral locations of small earthquakes that occurred within 3 days before and after magnitude 2.5 event of July 27, 1971. Bars indicate errors in epicentral locations; no bars denote locations with errors smaller than size of symbols. Notice that main event is at one end of the focal region. Triangles show seismograph sites, and arrows indicate direction of sites outside area of figure. N 78° E is a line perpendicular to the strike of fault plane as inferred from focal mechanism[3] and is trend of vertical section in Fig. 6. Insert shows location of BML area in New York State.

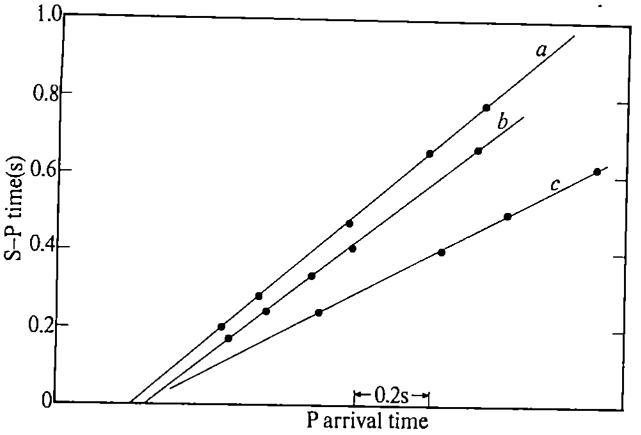

Fig. 2 S-P times as a function of P arrival times at various stations for three earthquakes. The slope gives (v_p/v_s-1) and the intercept $(S-P)=0$ is origin time of earthquake. Notice the small scatter (0.1 s or less) in data points from straight lines, and marked variation in v_p/v_s ratio. *a*, July 8 (1946), $v_p/v_s=1.84\pm0.04$; *b*, July 27 (1315), $v_p/v_s=1.77\pm0.03$; *c*, July 6 (2234), $v_p/v_s=1.52\pm0.05$.

for single shocks is the near absence of surficial sediments; gneiss outcrops widely in this area. Fig. 2 demonstrates marked variations in the v_p/v_s ratio for the three events and gives the range of S-P times, 0.15 to 0.8 s (that is, epicentral distances of about 1.0 to 6.5 km).

Changes in v_p/v_s

Figs. 3 and 4 show individual determinations of v_p/v_s as a function of time before and after the July 10 and 27 events, two of the largest shocks in the swarm. Arrows indicate the time of occurrence and relative size of all events larger than magnitude 1. In both Figs. a pronounced, broad minimum of a few days duration in v_p/v_s occurs before each of the two largest earthquakes. From July 1 to 3 and July 11 to 12 (Fig. 3) during which period no shocks larger than magnitude 1 occurred, the velocity ratio does not change appreciably from 1.75 (a Poisson's ratio of 0.26). Similarly, the ratio did not change significantly from 1.75 over a 7 day period in August (Fig. 5) during which time no shocks larger than 1 occurred. The largest (1.9) and smallest (1.52) velocity ratios in Figs. 3 and 4 differ by 22%.

Pronounced minima of a few hours duration seem to precede some shocks as small as magnitude 1.2 (Figs. 3 and 4). Minima for two shocks of magnitude 1.8 on August 14 (not shown) are nearly identical to that of the magnitude 1.8 event of July 9 (Fig. 3). Although minima were not detected before several other shocks of magnitude 1 to 1.5 (Figs. 3 and 4), the sparse data sampling may have missed rapid fluctuations in v_p/v_s.

Fig. 6 shows a vertical section perpendicular to the strike of the fault plane as inferred from a composite focal mechanism solution[3]. The section indicates positions and depths of those small shocks in Fig. 1 that occurred within three days of the magnitude 2.5 shock of July 27. The v_p/v_s value beside each earthquake shows no apparent correlation with either depth or position; neither do they vary significantly with azimuth or station location.

Semonova[2] found that the time duration of a pronounced minimum in v_p/v_s before earthquakes in Central Asia was proportional to the magnitude but that the percentage decrease was not a function of magnitude. The time duration of the pronounced minimum in velocity ratio for our data and that of Semonova[2] increases with increasing magnitude (Fig. 7). It is not clear, however, whether magnitude is a linear function of time as Semonova proposes or of log time as Fig. 7 might suggest. In any case extrapolation to larger magnitudes gives durations of months or longer for events of magnitudes greater than 6. Using a magnitude-fault length (*L*) relationship derived for California earthquakes[4] and assuming a linear relationship in Fig. 7 between log time and magnitude, we obtain time duration proportional to $L^{1.6}$.

Causal Mechanism

The earthquakes at BML and those in Central Asia for which large changes in velocity ratio were found are similar in several ways. Focal mechanisms are of the thrust type and the depth of focus is shallow. The depths of the events we studied were less than 2 km while most of those in Central Asia were less than 10 km. The seismic signals of BML events are rich in high frequencies. This may be indicative of high stress although efficient propagation alone may explain the enrichment of high frequencies. It is not unreasonable that thrusting related to continental collision in Central Asia may also be typified by high stress. Thus, it is not certain if similar changes in velocity ratio occur in other

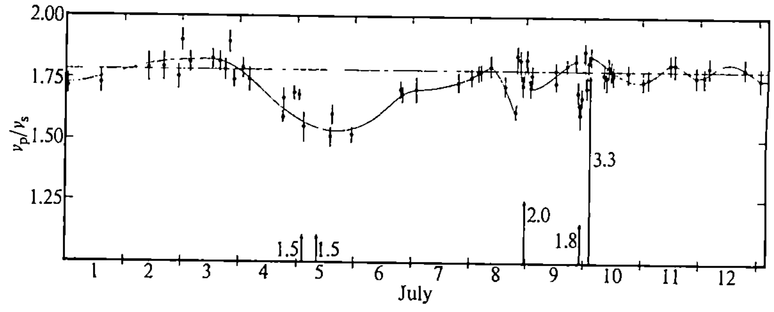

Fig. 3 Velocity ratio v_p/v_s as a function of time for series of small earthquakes before and after the largest event studied (July 10, 1971, magnitude 3.3). Vertical bars indicate ±s.d. in v_p/v_s measurement, arrows and numbers indicate the magnitude and time of occurrence of all events larger than magnitude 1 from July 1 to 12, 1971. Notice pronounced minimum in velocity ratio from July 4 to 8 that we tentatively associate with largest event on July 10; similar minima a few hours before smaller shocks on July 8 and 9 of magnitude 2.0 and 1.8; and the comparatively constant value of v_p/v_s before July 4 and after July 10 when no events larger than magnitude 1 occurred.

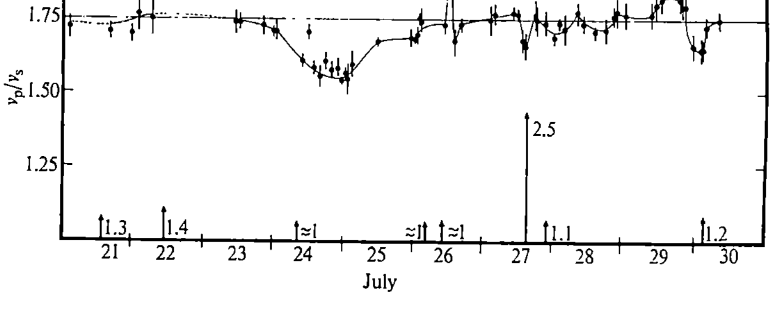

Fig. 4 Velocity ratio v_p/v_s as function of time before and after event of July 27, 1971, of magnitude 2.5. Symbols as in Fig. 3. Notice duration of minimum in v_p/v_s, which we associate with larger earthquake on July 27, is similar to that for event of magnitude 3.3 in Fig. 3. Minimum on July 29–30 may be related to event on July 30. No minima were detected before shocks on July 21, 22 and 24 but sampling may be too sparse to detect short fluctuations in v_p/v_s. Two anomalously high points on July 26 are associated with epicentres nearest the northwestern end of focal region in Fig. 1.

areas of dissimilar tectonics or rock type or where the focal depths are not quite as shallow. Nonetheless, the tectonic style in other areas such as in south-central Alaska and the Transverse ranges of California is similar in many ways to that in the above two areas.

It is indeed surprising that changes as large as 13% in velocity ratio occur in such a short time before small to moderate size earthquakes. This time is very short compared with what is normally thought to be the period of strain build-up in the Earth but is long compared with that for seismic wave propagation. Thus, it seems necessary to appeal to phenomena such as pore pressure variations, fluid flow, crack formation or creep that have appropriate time constants.

Increased pore pressures are known to be associated with several natural and man-induced earthquakes. Nur and Booker[5] suggest that aftershocks of natural earthquakes and of large underground nuclear explosions may result from a redistribution of pore pressure and fluid flow along faults. Assuming that fluid flow may be approximated by a diffusion equation, they obtain a time constant (τ) proportional to a characteristic length (L) squared. For $L=1$ km they obtain $\tau=1$ day for fractured and jointed rock. These values are comparable to the aftershock dimensions (Figs. 1 and 6) and to the time duration of minima in velocity ratio for BML shocks of magnitude near 3. The exponent 1.6 obtained earlier in the relationship of time duration of the velocity ratio minimum and fault length is intermediate between that for solutions to the wave equation (1.0) and that for fluid flow by diffusion (2.0). Nason and King[6] report creep events on the San Andreas fault that propagate with velocities of 0.5 to 6.0 km day^{-1}. Johnson *et al.*[7] correlate water fluctuations in a well in the San Andreas fault zone with creep events. Thus, fluid pressure variations and propagation of creep satisfy the time constants and fault dimensions obtained for BML and Central Asian events.

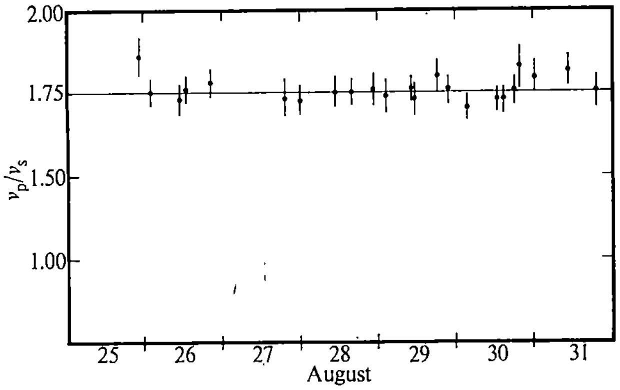

Fig. 5 Velocity ratio as function of time for 7 day period in August 1971 during which no earthquake of magnitude ≥1 took place. Symbols in as Fig. 3. Notice the absence of pronounced changes in ν_p/ν_s such as those in Figs. 3 and 4.

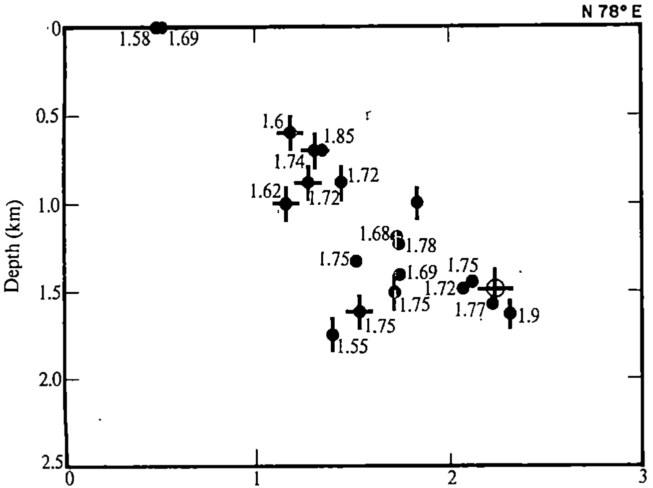

Fig. 6 Vertical section through hypocentral zone parallel to section line in Fig. 1. Data same as Fig. 1. Values of velocity ratio ν_p/ν_s shown beside solid circles that denote individual earthquakes. Bars indicate errors in location; no bars indicate errors were smaller than size of circles. Notice absence of any apparent correlation between the values of ν_p/ν_s and the focal depth. Note largest shock in this sequence (open circle) is located at down dip end of focal region.

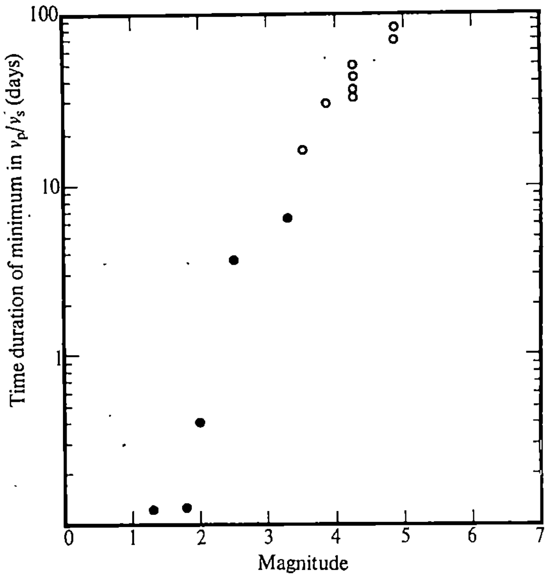

Fig. 7 Time duration of minimum in velocity ratio (measured from onset of minimum to time of earthquake) as function of magnitude. Solid circles are BML data and open circles are for Central Asia[2].

It is interesting to note here that the two largest events in the swarm on May 23, 1971, occurred two days after an extremely heavy rainfall that resulted in a rise of about 25 cm in the level of BML[3]. Foreshocks, however, were observed well before the rainfall. Thus, it is unlikely that this very small pressure change could have acted as anything more than a "last straw".

Gupta[8] reports small decreases in P and in S velocities before shear failure in laboratory tests. If P and S velocities both decrease or both increase but by different amounts, percentage changes in P or S much larger than 13% must be involved for BML events. Scholz[9] reports microfracturing and dilatancy (decreased volumetric strain) accompanying crack growth in rocks deformed in laboratory experiments. These effects become very pronounced within a few percent of the fracture strength of the rock. The presence of cracks drastically reduces the P and S velocities of dry rocks for confining pressures (or effective stresses) below about one kbar[10]. When these cracks are filled with water, however, the P velocity is not reduced as drastically for low confining pressures, whereas the shear velocity still decreases markedly at low confining pressures and is nearly the same as in dry rocks[10]. Thus, pronounced and rapid changes in the P to S velocity ratio at low effective stress can arise from changes in effective stress caused by crack development or changes in pore pressure for saturated rocks; or the rock passing from a saturated to unsaturated environment or vice-versa. The second alternative, however, seems to be less probable for BML because nearly all of the earthquake foci are likely to be below the water table.

The premonitory minima observed at BML and in Central Asia consist of a decrease in velocity ratio followed by an increase before the earthquake. We tentatively associate the decrease in velocity ratio with the rapid growth of cracks which leads to increased dilatancy, a drop in pore pressure, an increase in effective stress, and a more rapid increase in v_s than in v_p. The increase in velocity ratio is more difficult to explain but may be related to a subsequent increase in pore pressure as fluids either propagate along newly connected cracks or permeate into cracks from the surrounding medium. This model is consistent with Brace and Martin's[11] observation that strength is a marked function of strain rate for rocks of low porosity and permeability. Observations of changes in fluid pressure and perhaps of changes in radon exhalation (as observed before the Tashkent earthquake of April 26, 1966, see ref. 12) as a function of time should provide a check on our model.

With our present data we cannot ascertain whether changes in P, S or both velocities are responsible for the observed changes in velocity ratio. Nevertheless, the changes in v_p/v_s are large enough that small explosions should be useful in ascertaining how individual P and S velocities change and in checking the results obtained from earthquakes. Repeated explosions may provide a means of monitoring v_p/v_s and of predicting earthquakes in areas where it is not convenient or possible to use small earthquakes.

Very many more data from BML remain to be analysed. Some time after July 27 the maximum depth of earthquakes increased from 2.0 to 3.5 km. This apparently extended the rupture zone down dip to the east. The focal mechanism of these deeper events, while remaining of the thrust type, involved a significant change in the direction of maximum compressive stress compared to that for the shallowest shocks[3]. In a few cases the velocity ratio varies as a function of epicentral distance. We were surprised that this effect was observed for only a few percent of the shocks analysed. This suggests that the epicentral distances of our stations were still close to the strained region for most events. Perhaps the most perplexing observation is that the percentage change in velocity ratio is nearly the same for large or small shocks even though we presume the rupture lengths are quite different in size. We plan to analyse these effects in more detail.

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Cyclical Changes in the Habitat and Climate of an East African Ecosystem

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Ecological changes in an East African Game Reserve may be attributed to changes in climatic conditions and soil salinity. Tree damage from elephants and overgrazing by livestock are probably secondary factors.

Maasai Amboseli Game Reserve has suffered extensive loss of the fever tree (*Acacia xanthophloea*) woodlands over the last two decades. The decline was accompanied by a marked shift towards a more arid habitat, with overgrazing by Maasai livestock frequently regarded as the principal cause[1]. An alternative hypothesis links the changes to the elephant destruction problem, widespread in other East African Parks and Reserves, for example Tsavo, Murchison Falls and Manyara. Laws[2,3] suggests that these elephant-induced habitat changes stem from the disruption of local populations caused by human encroachment. Here we describe the magnitude of causes of woodland and other habitat changes in Amboseli. We also demonstrate the need for a long-term perspective of these changes, important to the future management of Amboseli and possibly habitat changes in other East African ecosystems.

The area concerned, the Amboseli basin, has been briefly described[4] and is the site of a lake that formed during the Pleistocene and dried out in the Recent epoch[5]. Rainfall averages 350–400 mm per annum supporting a dry savannah, bushed grassland[6]. Fever tree woodlands which formerly covered much of the basin area until the mid-1950s are generally associated with a high ground water-table. To evaluate the extent of changes within the woodlands, thirty random 18 hectare plots were drawn on a mosaic of 1950 aerial photographs and replicated on 1961 and 1967 mosaics. The sign test showed a significant decline between each of the data points ($P < 0.001$) with an 11% loss from 1950 to 1961, reaching 70% by 1967. Allowing for a bias of counting dead standing trees which constituted approximately 60% of the standing trees in 1967, we estimated that some 90% of the woodland trees were lost over this period, largely in the last decade.

In seeking the causal agents of "die-off" we recorded on the ground the condition of 20 or more trees in 18 stands, together with the incidence and level of elephant damage. Condition was estimated from the ratio of dead or moribund to intact major branches. In each stand soil samples were collected at 30 cm intervals down a profile 180 cm deep, or until the hardpan was reached. Textural and chemical analyses were obtained for each sample. The distribution patterns of Maasai settlements and livestock were available on a monthly basis over a 3 year period from 1967 to 1970[4].

The progressive increase in the number of dead trees towards the centre of the basin was negatively correlated with the density of livestock (Fig. 1). Also the area of highest woodland mortality has been a wildlife sanctuary from which livestock have been excluded since 1961, before the major decline of trees. Similar areas around the Reserve headquarters at Ol Tukai have been stock-free since 1947. Conversely, the basin-edge woodlands which have suffered least loss have, for various reasons, been the areas of highest settlement and cattle density for decades, which does not support the hypothesis that livestock are responsible for the habitat changes.

Elephant damage is extremely conspicuous; over 83% of trees examined showed some degree of debarking, although less than 1%, mainly young trees, had been pushed over. Debarking might impair water transport in the conducting tissue and result in death through "ring barking"; this was observed in a few cases where most of the stem was debarked. No statistically significant correlations were found between either individual tree condition or general stand condition and the incidence of elephant damage ($P > 0.1$). A substantial contribution to the variance was probably due to differential regeneration in trees of different ages. By taking height class as an approximation to age class and plotting the mean condition of each against the incidence of elephant damage, it was possible to reduce this source of error. The relationship of elephant damage to tree condition then appears highly correlated ($r = 0.80$, $P < 0.02$). Two observations, however, lead to the conclusion that elephant damage is not the sole or even primary cause of death, but amplifies other causes of death. First, 17% of all dead or dying trees were undamaged by elephants. Second, the mean condition against height-class curve was highly correlated for both elephant damaged and non-damaged trees ($r = 0.956$, $P < 0.001$), although the latter were in significantly better condition ($P < 0.05$).

An analysis of the soil samples showed that tree stands in an advanced stage of collapse were associated with highly saline soils, while healthy stands were associated with non- or mildly saline soils (Fig. 2). A fairly narrow margin around an EC_e of 8 mmho cm^{-1} divided healthy and moribund stands. In some cases dead stands were associated with EC_e values of 50–70 mmho cm^{-1}, equivalent to an osmotic pressure of approximately 25 atmospheres. Such high moisture tension can be expected to inhibit water uptake in most plants, with the exception of a narrow spectrum of halophytes[7]. *Acacia xanthophloea*, a hydrophyte[8], would not be expected to fall into this category.

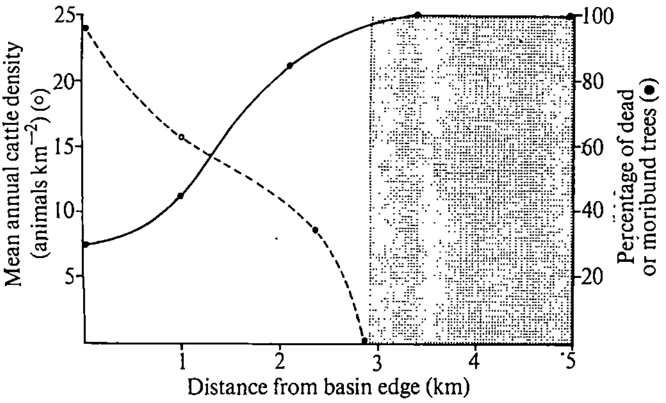

Fig. 1 The distribution of woodland mortality across a section of the Amboseli basin shows a progressive deterioration toward the centre. Cattle density, determined from monthly counts over three years, shows a reverse trend. The stock-free area (tinted) provides a useful control, demonstrating that livestock have had little influence on the major habitat changes.

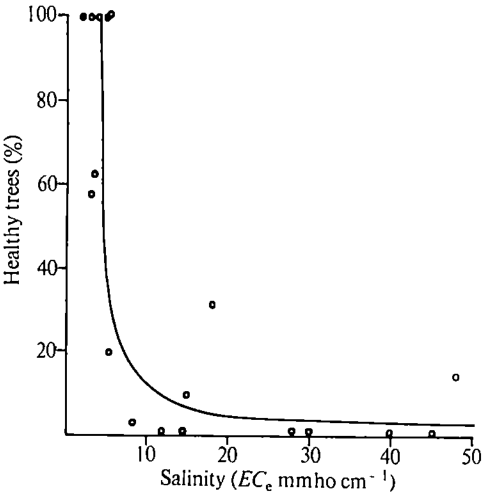

Fig. 2 For each sample plot, the percent healthy trees are plotted against the highest salinity values recorded from profiles taken through the rooting zone. In general, plots associated with an $EC_e < 7$ mmho cm^{-1} were in a healthy state, while those associated with an $EC_e > 8$ mmho cm^{-1} were in an advanced stage of collapse.

Evidence for this conjecture was derived from an examination of a dead stand of trees >12 m in an extremely saline area. The only regeneration was composed of saplings <2 m of which the taller individuals were dying. Analysis of the rooting system of these trees showed withering from the tips at about 40 to 60 cm depth, which from the soil profiles was found to correspond to a band of high salinity, 40–50 EC_e. The withering suggests tissue plasmolysis and eventual death through physiological drought on the highly saline soils. Less than 40% of these saplings showed any browse or elephant damage.

A highly significant correlation ($P < 0.001$) was also found between tree density and salinity (Fig. 3). The increasing level of salinity towards the basin centre probably explains the mortality pattern of trees noted earlier (Fig. 2), as there is a significant correlation between the two trends ($P < 0.02$).

With the available evidence strongly indicating salinity to be the primary cause of woodland mortality, it is necessary to offer some reason for the rapid and widespread salinization of Amboseli basin. The most likely explanation is an upward shift in ground water levels of some 3.5 m between 1961 and 1964, observed at Sinya Meershaummine[9], located in the basin. Borehole records at Ol Tukai Lodge demonstrate a similar elevation to a rest height of about 3–4 m below the surface.

The high correlation of both tree condition and density with soil salinity and the associated habitat changes mentioned below suggest it is unlikely that *A. xanthophloea* death results directly from drowning except along the swamp margins. Instead, a 3 to 4 m elevation in water-table has caused the capillary fringe to introduce a high level of soluble salts into the rooting layer, causing death through physiological drought. Russell[10] and More[11] have discussed the mechanisms of salinization due to a rising water-table or capillary fringe, and this is recognized as a common problem in irrigation engineering[12].

Lahi[9] and Bargman[13] have shown that increments in ground water level in Amboseli correlate with a post-1960 rainfall increase, while Campbell[14] indicated a less marked rise in water levels in the 1950s. It seems possible therefore to trace the woodland mortality ultimately to changes in the rainfall regime.

The Amboseli ecosystem is apparently sensitive to changing climatic conditions. A successional series of plants is apparent within the basin and, although the disappearance of fever trees is probably the most obvious feature of recent changes, the associated flora shows a comparable shift to halophytic species. The most conspicuous saline indicator is *Suaeda monoica* which is rapidly spreading across the basin as the woodlands decline. *Suaeda* cover was found to be inversely correlated ($r = -0.76$, $P < 0.001$) with *A. xanthophloea* across

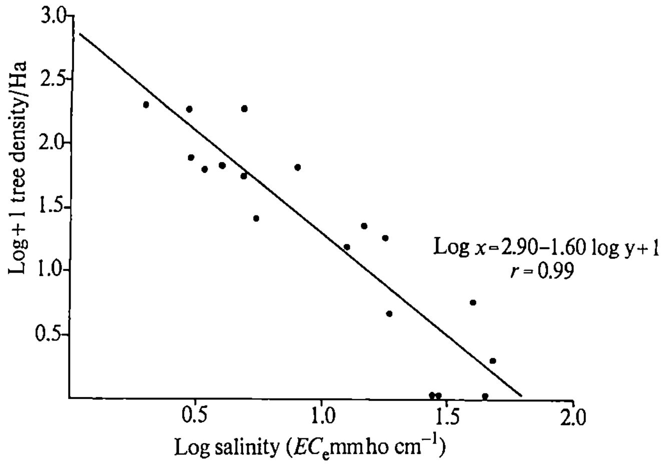

Fig. 3 Tree density for each plot was determined from aerial photomosaics, salinity as in Fig. 2. A sharp inflexion point at about 7–8 EC_e divides sparse from dense stands when plotted on a normal scale, but transformation to a log scale above gives a straight line correlation.

a section of receding woodland, the spread of *Suaeda* showing up clearly on the 1950 to 1967 aerial survey. Any major shift in water-table is likely to alter the salinity profile and affect successional series. A depressed rainfall period will result in a lowering of water levels, downward leaching of soluble salt and a shift to a non-halophytic vegetation, the converse with higher rainfall regimes.

On this basis it might be expected that a halophytic community dominated the basin during the last century when rainfall and lake levels were apparently higher[15]. Two lines of evidence support this hypothesis. First the Maasai record that during the period when the Nyanjusi I age-set were warriors the woodlands were almost non-existent and the swamps were far more extensive than at present. Jacobs[16] age-set chronology shows that this occupied the period between 1851 and 1871. According to the Maasai, two small groves of woodland then existed, separated by *Empaash* (Maasai, a corridor). With the woodlands now largely dead or moribund, *Empaash* divides two of the few remaining healthy groves. Secondly, descriptions of Amboseli given by early explorers make no mention of extensive woodlands. Thomson[17], who passed through in 1883, mentions a few "straggly trees", but no extensive woodland, while Volkens[18] described the area as dominated by *Suaeda monoica* as did Wickenburg[19]. A number of other references suggest that the area was sparsely wooded but covered by more extensive swamps. The now seasonal Lake Amboseli was apparently permanently inundated until the the 1920s[20]. Available photographs show a relatively young woodland in the 1930s, which, coupled with the preceding evidence, suggests that the major spread of woodlands did not begin until the end of the last century or, more possibly, early this century.

The change from a hydrophytic, dense woodland to a halophytic community has resulted in a sparse xeromorphic habitat, typical of more arid conditions. This fostered the view that the area was becoming more arid due to livestock overgrazing. It has also accounted for a pronounced shift in large mammal composition for which substantial information is now accumulating.

The most obvious change has been a decline in woodland-associated species such as lesser kudu, baboon, vervet-monkey, leopard and impala. Elephants appear to play a catalytic role in the present habitat changes rather than their primary role in other areas[3]. The incidence of elephant damage was found to be inversely correlated with woodland density (r=0.931, P<0.001). This relationship effectively accelerates the decline already under way as a result of salinization. It also results in the highest incidence of elephant damage being associated with the sparser and more moribund stands of trees, an association that has been readily interpreted to support the hypothesis that elephants are the primary agent of destruction.

The correspondence of the large oscillations noted over the last century in a number of East African lakes such as Victoria, Nyasa, Rudolf, and Naivasha, has been attributed to climatic changes[15,21,22]. The major fluctuations in the Amboseli ground-water and swamp levels follow a similar periodicity, with high levels pre-1890 and post-1960 and an intervening low. In Amboseli these changes have also had a pronounced influence on the entire ecosystem, demonstrating the need for a long-term perspective of the contemporary habitat changes. It is important to consider the effect of climatic shifts on other East African habitat changes, particularly closed drainage systems such as Manyara, Naivasha, Nakuru and Ngorongoro, and possibly on changes in elephant range and activity.

A long term perspective of contemporary habitat changes is especially relevant to the future management of Amboseli. Over the next decade or so, it is envisaged that investments in the basin will exceed K£1.5 million on the assumption of deriving annual tourist revenues ultimately reaching K£1.5 to 2 million[23]. In view of the recent hydrologic changes, it is important to consider the probability of investment loss through flooding, a further rise of the magnitude observed over the last decade would inundate most of the present lodge installations. It is imperative to plan developments and devise management strategies with some idea of possible future changes, because it is not economically feasible to control either the direction or magnitude of water-table shifts. A study of Holocene to present day lake and swamp level fluctuations of the type recently conducted by Butzer[21] and Butzer *et al.*[22] would help to elucidate the fluctuations and recurrence intervals that can be expected. An abundance of fish and mammalian fossils through a range of exposed strata in the basin, and a series of possible strand lines, offer ideal material for such a study.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Soft X-ray Pulsations from PSR 0833–45

THE radio pulsar PSR 0833–45 has the second fastest period of the presently known pulsars and was the first pulsar to be associated with a supernova remnant[1]. The SNR is the site of the nonthermal radio source[2] Vela X and has also been observed to be a region of soft X-ray emission[3]. We have recently observed the X-ray structure of the Vela and Puppis SNRs in the energy range 0.1–1.5 keV with a scanning focusing collector that provided substantially better angular resolution than did the previous soft X-ray measurements of this region[3]. The instrument was an improved version of the device described by Gorenstein *et al.*[4] and was flown aboard an Aerobee 170 sounding rocket fired from the White Sands Missile Range on April 1, 1972. We find the X-ray source in the Vela SNR to consist of a continuous extended region with structure plus a concentration of X-ray emission which is consistent with a point source at the position of PSR 0833–45. Here we report only results pertaining to PSR 0833–45.

The field of view of the instrument (1.8° × 12°) was divided into several image elements by a thin window position sensitive proportional counter in the focal plane. In the focusing direction, the response of each element was essentially rectangular, as determined by the 0.3° counter-cell width, because the mirror resolution was finer than this (~0.1°). In the other direction, the mirror plates behaved as a slat collimator with a 6° FWHM response. Data from the various image elements have been superimposed as prescribed by the aspect data.

In Fig. 1 we show the counting rate for the energy range 0.5–1.5 keV as a function of angle during a scan along a great circle that was approximately parallel to the galactic equator but displaced by several degrees. Several features are present in the 0.5–1.5 keV data. The Puppis SNR (Pup A), which is not related to the Vela SNR, is a rather bright X-ray source with a finite angular extent that is larger than our resolution. The X-ray source in the Vela SNR consists of an X-ray nebula that is not resolvable into point sources plus a peaking of the intensity at the position of PSR 0833–45 that to within our angular resolution is consistent with a point source. The Vela SNR radio source appears in some catalogues of radio sources as three sources, Vela X, Y, Z, and in other catalogues simply as Vela X. The radio features of Vela X, Y, Z do not necessarily have a one to one correspondence with features of the X-ray source which we will call the Vela X-ray Nebula. The position of PSR 0833–45 is about two degrees removed from centre of the Vela X-ray Nebula.

For the 0.5–1.5 keV energy range the intensity of the feature at PSR 0833–45 above background of the nebula is equal to 6.2±2.6% of the intensity of the entire Vela X-ray Nebula. This was determined from Fig. 1 as follows: the strength above background (dashed line) of the nebula was calculated assuming a ~6° region centred at a relative azimuth of ~4°. The two bins at the PSR 0833–45 arrow were reduced by a local nebula contribution (averaged over azimuth ~3.5° to 6.5°) to give an estimated strength of the pulsar. The quoted error is the statistical component only; there is a systematic uncertainty in determining background from the nebula in the vicinity of PSR 0833–45.

Our value of ~4×10^{-9} erg cm^{-2} s^{-1} for the integrated intensity (0.5–1.5 keV) of the Vela X-ray Nebula is in agreement with the report of Seward *et al.*[3]. For the energy range 0.1–0.3 keV there is no indication of an increase in intensity at PSR 0833–45 with the 3σ upper limit (4.5% of the intensity of the Vela X-ray Nebula). Thus the X-ray spectrum from the direction of PSR 0833–45 seems to be harder than the spectrum of the Vela X-ray Nebula. This conclusion is consistent with observations from Uhuru above 2 keV where there does seem to be localized X-ray emission about the position of PSR 0833–45; the Vela X-ray Nebula (except possibly for isolated fragments) is not detectable in the Uhuru energy range[5].

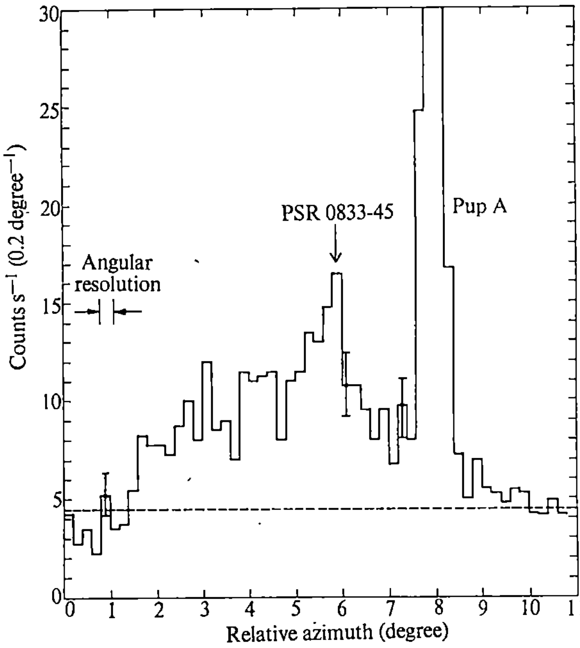

Fig. 1 Angular structure of 0.5–1.5 keV X-rays during scan along galactic equator. The dashed line is the background level outside of the Vela-Puppis region. The bright X-ray source is coincident with the radio source Pup A. The region with a 6° extent is the Vela X-ray Nebula. The position of PSR 0833–45 is indicated.

We have investigated the temporal behaviour of X-rays from the direction of PSR 0833–45 to search for possible periodic pulsations. The data from the PSR 0833–45 vicinity (a region 0.3° × 12°) include 6 s of observation and a total of only some 200 counts, more than 4/5 of which could be accounted for by the sum of the contributions from the nebula and background. The period of the radio pulsar PSR 0833–45 at the time of the X-ray observation was 0.08922 s (Reichley and Downs, private communication) at 2,388 MHz. The result of folding the X-ray data about this period is shown in Fig. 2. One bin contains substantially more counts than the mean. On the basis of Poisson counting statistics, the probability that the effect we observe at the period of the radio pulsar is a chance occurrence is only $\sim 2 \times 10^{-3}$. We have also analysed our data for unsuspected instrumental periodicities over a wide range of periods and in doing so have verified that the occurrence rate of large deviations from the mean is no greater than expected.

The phase of the radio pulse at the time of the X-ray observation (derived from radio observations of Reichley and Downs made only 30 min before the rocket flight) has been corrected for an estimated $\sim$0.050 s propagation delay in the interstellar medium and is shown in Fig. 2 in comparison to the X-ray. There is a difference in arrival times of about 0.029 s between the purported X-ray pulse and the radio pulse. Assuming that there is no gross time synchronization error in the X-ray data records which we have failed to uncover, there are two possible interpretations for the timing discrepancy. First, the X-ray effect is spurious. We think this is unlikely on the grounds that the probability of observing such an effect by chance is rather small. Also there is the evidence for a point-like X-ray feature at the position of PSR 0833–45 which is distinguished from the Vela X-ray Nebula by a harder spectrum and a location removed from the centre of the nebula. The other interpretation is that the time difference has a physical basis. The difference could be due to the existence of an interpulse from PSR 0833–45. If so the main pulse would be strong at radio frequencies and weak in X-ray emission while the reverse would be true of the interpulse. This situation does occur to an extent in the case of NP 0531, the pulsar in the Crab Nebula, where the relative intensity of the main to interpulse varies from one region of the electromagnetic spectrum to another[6].

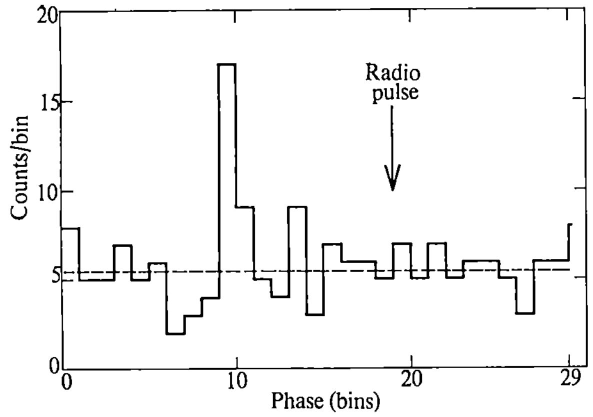

Fig. 2 Distribution in phase of counts detected from vicinity of PSR 0833–45 for an assumed period of 0.08922 s. The phase of the radio pulse is also shown. The dashed line is the average per bin excluding bin 10.

Relative to the Vela X-ray Nebula, the pulsed fraction inferred from Fig. 2 is about 2% in the energy range 0.5–1.5 keV. This is not in conflict with the previous upper limit of 1% reported by Seward *et al.*[3] at slightly lower energies because the pulsar is favoured relative to the nebula at higher energies. Further, the improved angular resolution of the present result entirely eliminates any contribution from Pup A. Thus the pulsed fraction of a point source at the position of PSR 0833–45 is about 1/3 but is subject to the systematic uncertainty described above. For the energy range 0.5–1.5 keV the time averaged intensity of the pulsed component is $7.4 \pm 2.8 \times 10^{-11}$ erg cm^{-2} s^{-1}. The intensity within the pulse is a factor of 30 ($2.2 \pm 0.8 \times 10^{-9}$ erg cm^{-2} s^{-1}).

If the X-ray pulsations are real, then in spite of the great difference in age and intrinsic diameter between the two nebulae there are several points of simularity between the relative intensities of PSR 0833–45 to the Vela X-ray Nebula and NP 0531 to the Crab Nebula. First, PSR 0833–45 has a harder spectrum than the Vela X-ray Nebula as does NP 0531 compared to the Crab[6]. In particular there is some evidence for emission from PSR 0833–45 above 23 keV (ref. 7). At these energies the Vela X-ray Nebula should no longer be detectable. Second, in both cases the X-ray luminosity of the nebula is about an order of magnitude smaller than the kinetic energy per second lost by the slowing down of a rapidly rotating neutron star whose rotation rate is equal to the pulsar period. Third, the time average of the beamed intensity of the pulsar received at the Earth is less than 10% of the intensity of the nebula in the energy range 0.5–1.5 keV but is a larger fraction at higher energies. One or more of these similarities may be coincidental. There is little doubt that essentially the entire X-ray luminosity of the Crab Nebula is due to synchrotron radiation from electrons accelerated to relativistic energies by NP 0531. Thus by analogy, one might ascribe the luminosity of the Vela X-ray Nebula to PSR 0833–45. But Tucker[8] has pointed out that under the conditions found in the Vela SNR at least part of the luminosity of the Vela X-ray Nebula could be thermally produced by the propagation of a blast wave in the interstellar medium. The Crab Nebula has not yet evolved to a stage where this process would be a factor in its X-ray emission.

The detection of pulsations, in addition to localized emission about PSR 0833–45, strengthens the case that the pulsar is a point source of X-rays. This should remove any residual doubt about its intimate connexion with the Vela SNR. The presence of pulsations also provides a basis for discriminating between various models of conditions in the vicinity of a rapidly rotating neutron star. The failure of intensive searches[9] to observe an optical counterpart for PSR 0833–45 implies that at visible wavelengths the Crab pulsar is at least 1,000 times brighter than the Vela pulsar, while at X-ray wavelengths it is only about twice as bright. This result favours pulsar models such as the one of Sturrock[10] in which a neutron star rotating three times more slowly than NP 0531 is still an active source of X-rays but emits no visible light. In this model the very low ratio of visible light to X-rays of PSR 0833–45 as compared to NP 0531 is a natural consequence of its longer rotational period.

We thank Drs P. Reichley and G. Downs of the Jet Propulsion Laboratory for providing timing data for the Vela pulsar, and Dr R. Giacconi for discussions. We acknowledge support from the Sounding Rocket Division of the Goddard Space Flight Center and the US Navy launch crew at the White Sands Missile Range. This work was supported by the Office of Space Science Applications of NASA.

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A Limit on the Redshift due to Interaction with Electromagnetic Radiation

IN a recent letter[1] Pecker *et al.* discussed the possibility that a part of the "cosmological" redshift could result from the interaction of photons with an interstellar radiation field. Although this suggestion is old[2,3], it has recently regained prominence with the discovery of the 3 K blackbody radiation. Pecker *et al.* discussed a formula for the energy loss of the propagating photon, ν_1,

$$-\delta\nu_1/\nu_1 = \Delta(\nu_2)n_2\delta l \tag{1}$$

where $\Delta(\nu_2)$ is the coupling constant between the propagating photon and the radiation field of frequency ν_2, n_2 is the number density (cm^{-3}) of the photons at ν_2, and δl is the length of the interaction path, in cm. Assuming that $\Delta(\nu_2)$ is independent of ν_2, they suggested an experiment to determine an upper limit for its value. The proposed experiment, measuring by the Mössbauer effect the energy loss of gamma rays traversing a laser beam, is very difficult to perform. But another Mössbauer experiment was performed a number of years ago to test just this question. In that experiment[4], gamma rays were propagated through a microwave cavity filled with photons of 9,234 MHz ($\lambda \approx 3$ cm) radiation; the fractional energy shift of the gamma rays due to the microwave field was found to be $0.4 \pm 6.0 \times 10^{-16}$, corresponding to a value of $\Delta(\nu_2) < 10^{-33}$ cm^{-1}. This limit is far smaller than the value $\Delta(\nu_2) \approx 10^{-30}$ cm^{-1} proposed in ref. 1 from the analysis of solar redshift data.

We note that the 3 cm wavelength of the microwave radiation used in the experiment of ref. 4 lies near the peak ($\lambda_{\max} \approx 0.1$ cm) of 3 K blackbody radiation. Thus the microwave experiment establishes a useful and reliable upper limit for $\Delta(\nu_2)$, provided the Doppler form of equation 1 is valid. This limit is far too small to account for the observed cosmological redshift which requires[1] $\Delta(\nu_2) \approx 10^{-30}$ cm^{-1}.

J. A. Giordmaine brought this problem to our attention; we thank J. R. Klauder for discussions.

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Consequences of a Universal Cosmic-ray Theory for γ-ray Astronomy

THE problem of the origin of cosmic rays is well known; but in spite of considerable advances in knowledge concerning energetic extra-terrestrial objects in recent years, no satisfactory solution has appeared. It is not clear, even, whether the important sources are within the Galaxy or outside it[1,2].

Here we consider the possibility of reviving a theory due to Hillas[3] in which the observed shape of the primary spectrum up to about 3×10^{19} eV is explained in terms of an evolving sources model with constant spectral index at production, and interactions with the microwave background radiation. Such a model can explain the sharp change of slope at 3×10^{15} eV inferred from measurements of the sizes of extensive air showers, as well as the high degree of isotropy which is maintained up to at least 10^{19} eV (ref. 4).

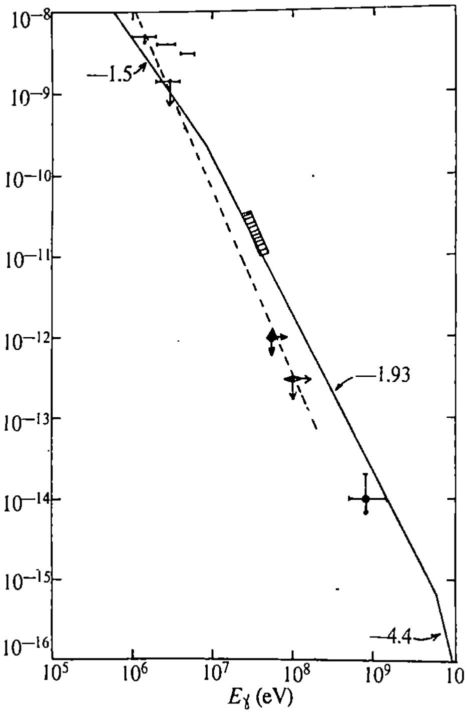

Fig. 1 The expected γ-ray spectrum (solid line). ◈, Ref. 9 (OSO-3); ⧫, ref. 8 (COSMOS-208); ✚, ref. 8 (PROTON-2); ⊢┬⊣, ref. 10 (COSMOS-163); ⊢⊣ ref. 11 (ERS-18); - - - - -, ref. 10 (E$^{-2.4}$ fit to experimental data); ▥, ref. 12 (balloon experiment).

The objections so far advanced to theories of this type seem to rely on assumptions concerning unknown astrophysical quantities. Thus the problem of a γ-ray excess due to pionization on intergalactic matter[5] can be removed by assuming a low enough density for the inter-galactic medium. An X-ray excess is clearly expected if the proton/electron ratio is equal to its local value, but in the absence of evidence to the contrary the possibility that this ratio may be large enough in metagalactic sources to remove the discrepancy cannot be ruled out.

A more fundamental objection would arise if it could be shown that the energy lost in forming the observed primary spectrum above 3×10^{15} eV (which appears initially in the form of electron pairs in this type of theory) will result in a γ-ray flux inconsistent with measurements of the diffuse γ-background. The mechanisms involved are inverse-Compton effect on the microwave background and pair-production on the starlight background, the latter occurring within the Hubble radius for γ-ray energies above about 10^{11} eV for reasonable estimates of the starlight background (see, for example, ref. 6). It is assumed that the starlight intensity does not increase with z—such changes as might be expected do not affect the results greatly in the energy range of interest to us (10^6 to 10^9 eV).

We have made calculations for a model in which the energetic cosmic rays are protons, with an energy spectrum on production of the form $G(E_p, z)dz = BE_p^{-\gamma} f(z)dz$, where B is a constant, z is redshift and $\gamma = +2.6$. The source efficiency $f(z)$ is taken as

$$f(z) = H_0^{-1} \frac{(1+z)^{\beta}}{(1+z)^2 (1+2q_0 z)^{\frac{1}{2}}} \quad \text{for } z < z_m$$
$$f(z) = 0 \quad \text{for } z > z_m$$

corresponding to the form used by Longair[7] in treating the evolution of powerful radio sources. In the calculations we took $q_0 = \frac{1}{2}$, although the results are insensitive to this parameter.

The proton spectrum expected at the present epoch after the generated protons have interacted with the microwave background has been calculated for various values of z_m and β. Comparison with the measured spectrum yields best-fit values $z_m = 14.3$ and $\beta = 4.3$. (The problem of predicted spectrum falling more rapidly above 10^{19} eV than observed is not considered here.) With these values the rather rapid change of slope of the the primary spectrum near 3×10^{15} eV is well represented.

The values for z_m and β can be compared with those derived by Longair from source counts ($2.3 < z_m < 4$ and $\beta = 5.7$ for density evolution, 3.3 for luminosity evolution). Our value of $z_m = 14.3$ is clearly inconsistent with the radio-source value but this is not catastrophic because cosmic-ray sources and radio sources need not evolve in the same time scale.

We show the expected γ-ray spectrum in Fig. 1. (The sharp changes of slope are consequences of approximations in the calculations.) Most of the energy is contained in the region where the slope is -1.93 so that the energy content per unit logarithmic interval is almost constant and the result is not very sensitive to the adopted parameters of the starlight spectrum.

Also shown are the experimental measurements of the diffuse γ-background from satellite and balloon experiments. The intensities measured by OSO-3, PROTON-2 and COSMOS-208 are clearly below the prediction of the present work. The measurements reported by Meyer-Hasselwander *et al.*[12] agree with our prediction.

On balance the observed intensities are too low and we conclude that what appeared to be a very attractive model is untenable. This conclusion will also apply to a "hybrid" model of the type suggested by Beresinsky and Zatsepin[13] in which galactic origin below 10^{15} eV is combined with a Hillas-type metagalactic spectrum above 10^{15} eV.

Note added in proof. Of course, if the "high" intensities of ref. 12 are confirmed by later work, then the conclusion will be reversed.

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Stability of CO_2 in the Martian Atmosphere and under Radiolysis

THE atmosphere of Mars appears to be predominantly undissociated CO_2 (refs. 1–3). It was possible by assuming very rapid transport downwards to explain the composition of the upper atmosphere, but a problem remained at lower altitudes. More recent determinations[4,5] of the rate of O–CO recombination have, however, given a rate constant two orders of magnitude lower than that used in the calculations for 200 K, the Martian surface temperature. This creates a more severe problem. There are less CO and O_2 than can be accounted for by a mechanism of photolysis and recombination.

$$CO_2 + h\nu \rightarrow CO + O \qquad (1)$$

$$O + CO + CO_2 \rightarrow 2CO_2 \qquad (2)$$

$$O + O + CO_2 \rightarrow O_2 + CO_2 \qquad (3)$$

$$O + O_2 + CO_2 \rightarrow O_3 + CO_2 \qquad (4)$$

$$O_3 + h\nu \rightarrow O_2 + O \qquad (5)$$

An earlier suggestion[2] that further reactions involving CO_3 could explain the results is not correct[1,3].

$$O(^1D) + CO_2 \rightarrow CO_3 \qquad (6)$$

$$CO_3 + CO \rightarrow 2CO_2 \qquad (7)$$

Furthermore, reaction (6) without a third-body or as a radiative process seems highly unlikely, and recent experiments yield no evidence for its existence[6]. It has also been shown that a pure CO_2 atmosphere is photochemically unstable under conditions where O (^{1}D) would be produced[7]. CO_2 does, however, show an apparent stability under reactor radiolysis[8]; isotope-exchange experiments have confirmed that both dissociation and recombination occur. Similar behaviour should be expected on Mars and it is pertinent to look for a common explanation.

The principal difference between photolysis and radiolysis lies in the production of ions under high-energy irradiation. The production of fragments and metastables would be expected to be somewhat similar in both cases. An ionic mechanism may therefore explain the recombination in CO_2. Although it has been shown[9,10] that earlier explanations of radiolytic stability based on negative-ion chemistry were unsatisfactory, positive-ion processes cannot be ruled out at the present time. It is known that, in the absence of CO_2, CO is rapidly oxidized by O_2 under irradiation, and the following mechanism has been proposed[11].

$$O_2^+ + CO \xrightarrow{M} CO_3^+ \qquad (8)$$

$$CO_3^+ + CO \rightarrow CO_2^+ + CO_2 \qquad (9)$$

$$CO_2^+ + O_2 \rightarrow O_2^+ + CO_2 \qquad (10)$$

In CO_2 the terminal positive ion under radiolysis is probably CO_4^+[10] and the existence of the same species in the Martian atmosphere[12] has been suggested. The following modified positive-ion mechanism could oxidize CO in the presence of CO_2.

$$CO_4^+ + CO \rightarrow CO_3^+ + CO_2 \qquad (11)$$

$$CO_3^+ + CO \rightarrow CO_2^+ + CO_2 \qquad (9)$$

$$CO_2^+ + O_2 \rightarrow O_2^+ + CO_2 \qquad (10)$$

$$O_2^+ + 2CO_2 \rightarrow CO_4^+ + CO_2 \qquad (12)$$

$C_2O_4^+$, clustered CO_2^+, probably also charge transfers to O_2 (ref. 13).

At altitudes below 70 km on Mars, the positive-ion density is 10^3 cm^{-3} (ref. 12) and the rate of oxidation of CO by positive ions will be $\sim 10^3\ (k_{11} + k_9)$ s^{-1}. The rate of production of CO by photolysis[1] $\sim 5 \times 10^5$ cm^3 s^{-1} to give a steady-state density of $500/(k_{11} + k_9)$ molecule cm^{-3}. The observed CO/CO_2 ratio is 0.1% and the CO_2 density falls from 2.25×10^{17} molecule cm^{-3} at the surface to 2.25×10^{15} at an altitude of 60 km, giving a CO density ranging from 2.25×10^{14} to 2.25×10^{12}. If any effects arising from transport are neglected, values of k_{11} and k_9 of the order of 10^{-10} cm^3 molecule^{-1} s^{-1} are needed to explain the observations. The radiolytic problem[10] calls for rates $> 10^{-12}$.

Further experimental measurements are needed to assess this mechanism. If k_{11} and k_{12} are found to be too small, then it would appear that minor constituents are responsible for promoting the oxidation of CO. Besides the well-established effect of H_2O at high temperatures, catalytic effects on CO oxidation arising from iron carbonyl[14] and perhaps also CH_4 (ref. 15) have recently been noted. Impurities also enhance the apparent rate of oxygen atom recombination with CO[5].

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Earth-Moon Mass Ratio from Mariner 9 Radio Tracking Data

THE navigation of the Mariner 9 spacecraft from Earth to Mars was performed using phase-coherent range and doppler tracking data recorded by the Jet Propulsion Laboratory (JPL) Deep Space Network. These data also determine the Earth–Moon mass ratio, which involves the following physics: as the Earth revolves about the centre of mass of the Earth–Moon system, a sinusoidal curve is impressed on the range and doppler tracking data with a frequency equal to the sidereal mean motion of the Moon. This signature is shown in Fig. 1, where a perturbation of 0.0003 was made in the mass ratio (μ^{-1} = mass of Earth over mass of Moon). This sinusoidal variation in the tracking data can be eliminated by finding a value for μ^{-1} that properly represents the amplitude of the barycentre motion of the Earth. The procedure is direct and for all practical purposes is completely uncoupled from other parameters used in reducing the tracking data.

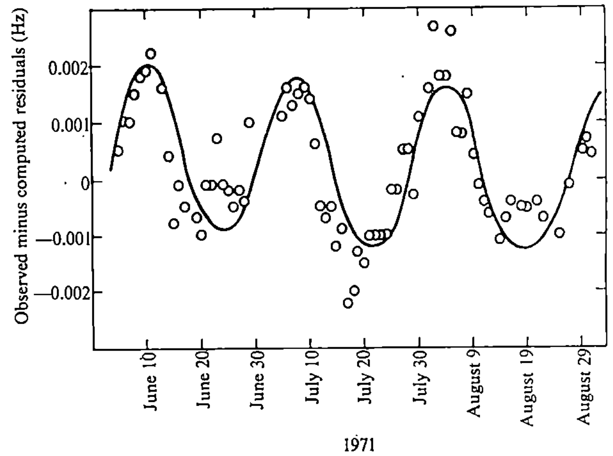

Fig. 1 The effect of Earth–Moon mass ratio on doppler residuals.

The mass ratio was determined from range and doppler data obtained over a period of 15 weeks (June 5 to September 15, 1971). The data coverage is shown in Table 1. We also show the statistics from the best determination. The data reduction was performed using the JPL Double Precision Orbit Determination Program[1], which uses a Cowell integrated trajectory and a batch least squares filter. In weighting the range data, we have taken extreme care to assure optimal data utilization without conflicting with the doppler data. The Mariner Mars 1969 results showed that such conflicts can cause significant perturbations in the estimated parameters.

The Deep Space Network has three types of ranging systems: Mu, Tau, and Mark 1A. The Mu and Tau systems are capable of planetary distances, whereas the Mark 1A ranging system is limited to an effective one-way range of approximately 10^7 km. In weighting the range data the following factors were taken into consideration. First, assuming no external errors, the Mu and Tau systems are accurate to about 20 m. This includes system noise and transponder and ground equipment calibration errors. The Mark 1A ranging system is accurate to about 30 m. Second, because the radio signals travel through the ionosphere of the Earth and the interplanetary space plasma, there is a change in the radio signal path length. The group wave path length is increased, while the phase wave path length is decreased, corrupting both range and doppler measurements made from the radio signal. The charged particles of the

Table 1 Tracking Data Statistics

Tracking station	Data type *	Number of points †	Data interval, 1971 (UTC)	Mean residual ‡	Root-mean-square residual ‡
Goldstone-Echo, Calif.	Doppler	1,069	6/5 08 : 37 to 9/14 04 : 59	0.000005 Hz	0.00144 Hz
	Range–Mark 1A	248	6/5 08 : 42 to 6/30 09 : 14	−17.73 RU	20.94 RU
	Range–Mu	31	7/12 05 : 40 to 9/6 02 : 49	−19.12 ns	134.55 ns
Goldstone–Mars, Calif.	Doppler	193	6/5 13 : 01 to 8/31 09 : 36	0.000002 Hz	0.00132 Hz
	Range–Tau	109	6/5 12 : 43 to 8/27 06 : 20	−33.67 ns	116.22 ns
Woomera, Australia	Doppler	1,638	6/5 01 : 15 to 9/12 17 : 56	−0.000012 Hz	0.00139 Hz
	Range–Mark 1A	594	6/5 01 : 09 to 7/13 17 : 40	5.28 RU	19.21 RU
Johannesburg, South Africa	Doppler	1,336	6/5 02 : 54 to 9/14 22 : 57	−0.000117 Hz	0.00140 Hz
	Range–Mark 1A	776	6/5 03 : 00 to 7/18 04 : 31	4.38 RU	20.60 RU
Cebreros, Spain	Doppler	387	6/26 00 : 43 to 9/12 00 : 36	0.000023 Hz	0.00188 Hz
	Range–Mark 1A	27	7/5 02 : 40 to 7/15 02 : 50	1.97 RU	21.04 RU

* Mark 1A = near-Earth ranging system; Tau and Mu = ranging systems using different ground hardware.
† Sample rate for doppler and range was 20 min.
‡ 1 Hz = 65 mm/s; 1 RU (range unit) ≈ 1 m; 1 ns ≈ 0.15 m.

Earth's ionosphere could account for as much as a 15 m error in range; the charged particles in the interplanetary medium (space plasma) could account for as much as a 22 m error in range (J. F. Jordan *et al.*, paper presented at AAS/AISS Astrodynamics Conference, August 1970). Third, another possible cause of range error is the Z component of station location. This component is parallel to the Earth's spin axis. The computed range value is sensitive to incorrect Z values when the probe declination becomes large in absolute value. An equation relating the two is[3]

$$\Delta\rho = \Delta Z \sin \delta$$

where ρ is the range datum and δ is the geocentric declination of the spacecraft.

Because previous space mission data did not yield significant information on the Z component of station locations, JPL analysts used the Z values obtained by the Smithsonian Astrophysical Observatory (SAO) in 1969. The change in the Z component was as much as 56 m. Assuming that the Z values from SAO may be in error by 30 m and the maximum absolute value in geocentric declination for Mariner Mars 1971 is 29.15°, the above equation would yield a range error of 14.6 m. The doppler data are insensitive to this Z-component error. Even though the Z component of a station location is not too well determined, the distances from the spin axis and the longitude are known to better than 3 and 5 m, respectively.

A number of solutions with different combinations of weights for each data type and different sets of estimated parameters were examined. The standard set of estimated parameters includes the probe position and velocity (6), solar pressure (3), attitude control leaks (3), station locations (15), and the Earth–Moon ratio (1). An *a priori* statistic of 0.0166 was applied to the mass ratio parameter. These solutions and their identifications are given as follows:

Case 1, Doppler only (doppler weight = 0.015 Hz) with standard estimated parameter set. Case 2, Range only (range weight = 100 m) with standard estimated parameter set. Case 3, Doppler and range (doppler weight = 0.015 Hz, range weight = 100 m) with standard estimated parameter set. Case 4, Doppler and range (doppler weight = 0.015 Hz, range weight = 100 m) with standard estimated parameter set plus Mars and Earth–Moon barycentre ephemeris parameters. Case 5, Doppler and range (doppler weight = 0.015 Hz, range weight = 50 m) with the estimated parameter set as in Case 4.

Solutions	μ^{-1}
Case 1	81.30068
Case 2	81.30067
Case 3	81.30067
Case 4	81.30067
Case 5	81.30068

All solutions yielded nearly the same mass ratio. Cases 1 and 2 give remarkable agreement on a mass ratio between the two data types. With such good agreement, the relative weight of the two data types becomes less significant. Cases 3 and 4 show that the lunar ephemeris error is probably too small to have an effect on the mass ratio estimate. Possible error sources are the periodic variations in the interplanetary medium. W. G. Melbourne has shown (12th Plenary Meeting of the Committee on Space Research, Prague, 1969) that a 28 day sinusoidal variation of solar flux of 0.1% could produce an error of about 0.001 in the mass ratio, but that it is not likely. Also, the agreement of mass ratios computed from the data gathered from several interplanetary spacecraft does not indicate this sort of systematic error unless the phase of the flux variation is the same for each mission, which does not seem likely.

Table 2 Estimates of the Earth–Moon Mass Ratio, μ^{-1}

Spacecraft	μ^{-1}	$\mu^{-1}-\overline{\mu^{-1}}$	Reference
Pioneer 8	81.3004 ± 0.0001	-0.0003	5
Pioneer 9	81.3008 ± 0.0001	0.0001	5
Mariner 2 (Venus)	81.3001 ± 0.0013	-0.0006	6
Mariner 4 (Mars)	81.3015 ± 0.0017	0.0008	7
Mariner 5 (Venus)	81.3013 ± 0.0002	0.0006	5
Mariner 6 (Mars)	81.3005 ± 0.0002	-0.0002	5
Mariner 7 (Mars)	81.3005 ± 0.0002	-0.0002	5
Mariner 9 (Mars)	81.3007 ± 0.0001	0.0000	

$\overline{\mu^{-1}}$ = arithmetic mean.

The results from the Mariner Mars 1971 data are given in Table 2 together with previous results obtained from Pioneers 8 and 9 and Mariners 2, 4, 5, 6 and 7. Values computed for Pioneers 8 and 9 and Mariner 2 were obtained from solutions using only doppler data. It is interesting to note that the Mariner 9 value and the mean of all spacecraft determined values of μ^{-1} are 81.3007. The deviations from the arithmetic mean of the Mariner and Pioneer values are tabulated in Table 1. Further, the mass ratio computed from the last five interplanetary spacecraft launched (Pioneers 8 and 9 and Mariners 6, 7 and 9) showed a spread of only 0.0004. The values for Pioneers 8 and 9 and Mariners 6, 7 and 9 are 81.3004, 81.3008, 81.3004, 81.3005 and 81.3007, respectively. This provides a good indication of the accuracy of μ^{-1}. The decrease in the fluctuation of the mass ratio value can be attributed to the improvement of data quality owing to changes in Deep Space Network tracking systems and the change in computer software from single precision to double precision.

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Predicting Light Flashes due to α-Particle Flux on SST Planes

The astronauts who flew on Apollo Lunar Missions 11 to 15 reported the observation of light flashes at a rate about one per minute when they were travelling outside the geomagnetic sphere of the Earth and their eyes were dark-adapted[1]. Experiments to determine the causes of the phenomenon[2-6] confirm that the flashes were caused either by direct interaction between energetic heavy primary cosmic rays or neutrons and the retina, or by Čerenkov radiation produced by muons. We have already reported[7] that the flux of stopping cosmic nuclei of medium and heavy charges at the levels at which SSTs fly (60,000 to 70,000 foot) is of the order of 10^{-4} [cm^2-min-ster-(MeV/n)]$^{-1}$ with a medium energy of about 120 MeV/n. If every nucleus in these categories could produce a flash in the human eye, the frequency of light flashes would be 2 to 3 per hour for an eye of 2.5 cm diameter subtending a solid angle of 2π radian. But it was noticed in the Berkeley experiments[8,9] that fast alpha particles (up to 240 MeV) did produce flashes and streaks when they stopped inside the eye or penetrated through the retina. Because the α-particle flux is much higher than that of heavy nuclei in primary cosmic rays, the possibility of observing light flashes on SST planes owing to α-particles cannot be ruled out. We have investigated data obtained from a US Air Force plane during 80 h of supersonic high altitude flight in 1970.

The plane, an RB-57F, carrying an emulsion-plastic stack, flew over Alaska during the non-flare period from June 19,

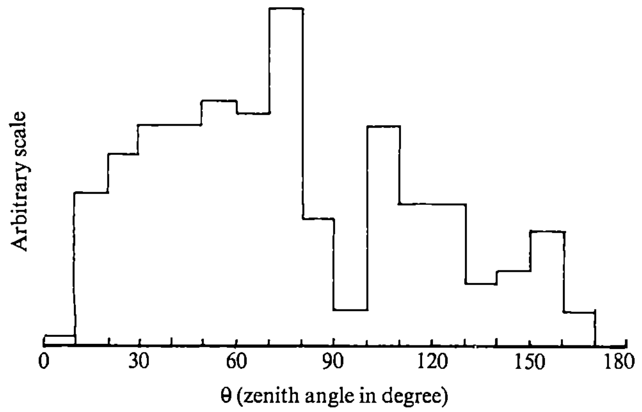

Fig. 1 Angular distribution of α-particle flux as function of zenith angle (θ).

1970 to August 10, 1970. The maximum geomagnetic cut-off rigidity was 0.1 GV. The flight time of the airplane at SST altitudes amounted to a little more than 53 h. The details of the flights have been described elsewhere[10].

The detector stack contained 48 plates of G5 emulsions, each 10 cm × 10 cm × 600 μm. Twenty-four plates in succession were under area-scanned for the ending tracks left by protons and α-particles. The relative abundance between the two categories was estimated by randomly selecting a number of tracks of an approximately equal length and identifying their charges by use of δ-ray counting.

Our results show that about one third of the stopping α-particles found in the stack ended within the top 6 plates. In terms of thickness of the human eye, filled with a vitreous fluid which is 98% water, we have estimated a total flux of about 0.7 α-particles $\text{mm}^{-2}\ \text{h}^{-1}$. If the cross-section of the eye is 500 mm^2, the total number of α-particles stopping in the eye would be 350 h^{-1}. But most of these particles would stop in the vitreous body, only 11 h^{-1} hitting the retina if the thickness of retina is 2.5 mm. If each α-particle stopping at retina can cause one flash, we expect to observe 11 flashes h^{-1} during the high altitude part of an SST flight.

In order to examine this problem from the energy point of view, we present the energy distribution of the observed α-particle flux in Table 1.

Table 1 Energy Distribution of α-Particles Detected at SST Levels

Energy (MeV)	α-particle flux (α-particles $\text{mm}^{-2}\ \text{h}^{-1}\ \text{MeV}^{-1}$)
20	4.30×10^{-3}
40	3.75×10^{-3}
60	3.45×10^{-3}
80	3.10×10^{-3}
100	2.60×10^{-3}

α-Particles with energy equal to or greater than 62 MeV can penetrate through the eye. If we assume that these α-particles can also induce light flashes, an SST passenger should observe 75 flashes h^{-1}. This sounds alarming.

We emphasize, however, that we have encountered a number of difficulties in carrying out the analysis. First, the proton background was too high. According to our measurements the ratio between α's and protons is about 1 : 12, which is of the same order as reported by McNaughtan[11] for an altitude of 90,000 foot. Second, the stack consisted of plastics and emulsions, which introduced inaccuracy to the energy estimation. Third, the α-particles seemed to have entered the stack from all directions (see Fig. 1). This might be due to the variable orientation of the aircraft during the flights. In view of these difficulties, our results can only be taken as a rough reference for more accurate measurements.

We thank Captain Philbrick of Kirtland Air Base for the flights, Emmanuel College Physics Research Laboratory for the preparation, processing and scanning of the stack (under an AFCRL contract), David Bushman and Nelson Thompson of Mississippi State University for the scanning, measurement and calculations, and W. Heinrich at Kiel for discussions.

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Differential Raman Scattering of Right and Left Circularly Polarized Light by Asymmetric Molecules

IT has been suggested that Rayleigh and Raman scattered light from optically active molecules should show polarization effects which could provide new information about their structure and configuration[1–3]. Circular intensity differentials (CIDs) defined by[2]

$$\Delta = (I^R - I^L)/(I^R + I^L)$$

where I^R and I^L are the scattered intensities in right and left circularly polarized incident light, have recently been observed in the Raman spectra of α-phenylethanol and α-phenylethylamine[4]. (Raman CID was first reported by Bosnich *et al.*[5], using α-phenylethylamine, but it has been suggested that the results are spurious[4].) Observations now reported on another liquid, α-phenylethylisocyanate, could indicate that these differentials originate in bending vibrations around the asymmetric carbon atom.

We have observed a large Raman CID couplet in α-phenylethylisocyanate, consisting of a positive and a negative component associated with two weakly polarized bands at ~223 cm^{-1} and ~313 cm^{-1}. The component of the light scattered at 90° and linearly polarized parallel to the scattering plane was sampled because, for reasons discussed previously[4], only this component was free of spurious contributions in our instrument. The peaks of the lower and higher frequency bands are associated with values of $|\Delta| \sim 2 \times 10^{-3}$ and $\sim 1.7 \times 10^{-3}$, respectively. Much smaller CIDs were found in other parts of the spectrum, including one at ~345 cm^{-1}. The (+)- and (−)-enantiomers give mirror image couplets. The CID couplets observed previously[4] in α-phenylethanol and α-phenylethylamine are associated with Raman bands in both molecules at ~315 cm^{-1} and ~365 cm^{-1} with values of $|\Delta| \sim 1 \times 10^{-3}$ and $\sim 0.5 \times 10^{-3}$, respectively.

Comparison with the Raman spectrum of CHFClBr[6] indicates that the two vibrations giving rise to the isocyanate CID couplets originate in a degenerate parent vibration in a

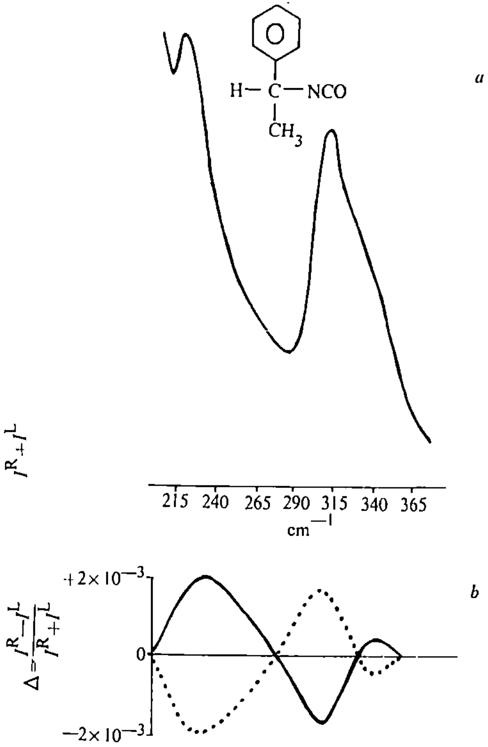

Fig. 1 Raman (*a*) and Raman CID (*b*) spectra of α-phenylethylisocyanate for scattered light linearly polarized parallel to the scattering plane. ——, (−)-enantiomer; . . . . , (+)-enantiomer. The background was subtracted from the Raman intensities in estimating Δ. The absolute value of Δ for the band at ~223 cm^{-1} is uncertain since the background is still large in this region. Raman spectrum, slit width 2 cm^{-1}; Raman CID spectrum, slit width 6 cm^{-1}.

molecule of higher symmetry (c.f. the generation of circular dichroism couplets in degenerate parent electronic transitions which are split by a lowering of symmetry). If the groups attached to the asymmetric carbon atom are regarded as atoms of equivalent mass, the vibrations around the asymmetric carbon atom in $CH(CH_3)(NCO)(C_6H_5)$ should have frequencies close to those of the nine fundamentals of CHFClBr. Thus CHFClBr has two fundamentals at ~225 cm^{-1} and ~313 cm^{-1} which originate in a doubly degenerate vibration in CHX_3 (ref. 6): these frequencies correspond closely to those at which the CID couplet occurs. Unfortunately this argument cannot be extended directly to $CH(CH_3)(OH)(C_6H_5)$ and $CH(CH_3)(NH_2)(C_6H_5)$ because only one of the frequencies at which the couplets occur coincides with the appropriate frequencies in the "equivalent" molecule CHF_2Br (~240 cm^{-1} and ~323 cm^{-1} (ref. 7)). Actually the fundamental at ~240 cm^{-1} was not observed in the Raman[8] spectrum of CHF_2Br, and no band was observed in this region in the Raman spectrum of $CH(CH_3)(OH)(C_6H_5)$ or $CH(CH_3)(NH_2)(C_6H_5)$.

These results indicate that a method exists for directly probing the stereochemistry of asymmetric carbon atoms, which is not possible with electronic optical rotatory dispersion and circular dichroism as chromophoric electrons are not delocalized over asymmetric carbon atoms. The larger CIDs in the isocyanate indicate that the effect is a function of the differences in the masses of the four atoms or groups attached to the asymmetric carbon atom or of the corresponding mass-weighed force constants. If so, Raman CID could provide a better criterion than rotatory power (which depends on subtle and sometimes unpredictable electronic effects) for correlating absolute configurations.

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Lift and Drag Measurements on a Hydrofoil in Dilute Polyox Solutions

The use of hydrofoils for a wide variety of purposes such as propeller blades on boats, as sailboat keels, ship rudders, submarine and torpedo fins, lifting surfaces of hydrofoil boats, and shroud ring stabilizers for missiles, has prompted efforts to increase the lift-to-drag ratio by various means. The favourable drag reducing effect of polymers, particularly for flows in pipes[1], suggests that they might be of value in increasing this ratio.

The experimental apparatus, described in detail elsewhere[2], consisted of a circulating water tunnel with a test section 10 cm by 20 cm; lift, drag, and pressure measuring devices; and a rheometer similar to that used by Hoyt[3]. The hydrofoil (NACA–0024), made of polished aluminium, was 10 cm wide, 10 cm long, and had a maximum thickness of 2.44 cm. The Reynolds number, based on the maximum thickness, ranged from 5×10^4 to 3×10^5. The polymer used in these studies was a high molecular weight additive, 'Polyox WSR–301'.

Appropriate amounts of polymer powder were sprinkled, over a few minutes, into the test section as the pump ran at its lowest speed, thus wetting and separating the particles. The friction-reducing effectiveness λ of the solution, determined with the turbulent-flow pipe rheometer and calculated from

$$\lambda = 100\,(f_t - f)/(f_t - 64/Re)$$

(f, friction factor for the sample solution; f_t, fanning friction factor for tap water), gradually decreased from 80 to 65 over a test period of approximately 1 h (ref. 4).

Lift, drag, and pressure distribution at the mid-plane were measured at the angle of attack settings of 0, 3, 6, 9, and 12 degrees at solution concentrations of 0, 1, 5, 25, 50, and 100 p.p.m.

The results are shown in Fig. 1 for a representative Reynolds number of 2×10^5. As can be seen, the lift consistently decreases with increasing concentration. At all Reynolds numbers from 5×10^4 to 3×10^5, even a concentration as small as 1 p.p.m. produced a reduction in lift. Also shown in Fig. 1 is the drag coefficient. At small angles of attack and within the range of concentrations tested, the drag coefficient remained nearly identical to that for water. At larger angles of attack, polymer solution flow yielded relatively larger drag coefficients. Thus it is apparent that the polymer (here we have to limit our conclusions to 'Polyox WSR–301') significantly decreases, relative to water, the lift-to-drag ratio of the foil tested.

The pressure measurements revealed relatively large amplitude oscillations particularly at the suction side of the foil. Flow visualization studies with dye (injected at various pressure taps) showed the existence of a large scale instability in the boundary-layer flow.

Although the foregoing results are based on a single type of hydrofoil, they are sufficiently consistent to tentatively conclude that the performance of hydrofoils is not likely to be improved by means of polymers. A similar conclusion has been arrived at by Wu[4] and Kowalski[5] in connexion with the effect of additives on propeller performance.

The reasons for the observed reduction in lift are not as

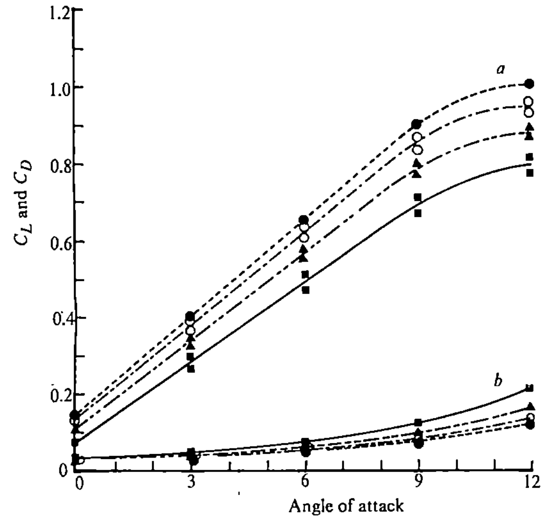

Fig. 1 Lift (*a*) and drag (*b*) coefficients as a function of the angle of attack. ●, Water. ○, 1 p.p.m.; ▲, 5 p.p.m.; ■, 100 p.p.m. polymer concentration. $C_L=2L/\rho AU^2$, $C_D=2D/\rho AU^2$. *L*, Lift force; *D*, drag force; ρ, density; *A*, lifting surface area; *U*, velocity of ambient flow. Both coefficients are corrected for the tunnel-wall constraint.

yet clear. Because the density and viscosity of the fluid are practically unaltered and the experiments are conducted at identical ambient flow velocities, the circulation about the foil must have been reduced by the polymer by some unknown mechanism. Finally, the large amplitude oscillations in wall pressure suggest that the polymer has a destabilizing effect on the external flow about bluff bodies. This latter conclusion is fairly well substantiated by extensive experiments carried out with circular cylinders in homogeneous polymer solutions at comparable concentrations and Reynolds numbers[6].

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Spherical Particles formed in Rolling Contact Fatigue

IN an investigation of fracture phenomena associated with rolling contact fatigue failure[1], it was suggested that spherical particles found on fractured bearing ball surfaces could be formed from tongues of metal removed by a cavitation erosion process due to the application and release of extreme pressure in the lubricant entrapped in the propagating crack by rolling contact. A correlation between cavitation erosion and rolling contact fatigue resistance has been established[2]. Loose pieces of metal could be severely worked by the pressure build-up in the lubricant entrapped in the fatigue crack or by pressure on the fracture faces during passage of the crack over the mating bearing surface. The mechanism of formation of the spherical particles and the possibility of their being artefacts[3,4] are uncertain. It has been reported[5] that similar spherical particles of debris are formed under specific conditions of fretting, and their formation by a process of deformation has been provided by scanning electron microscopy.

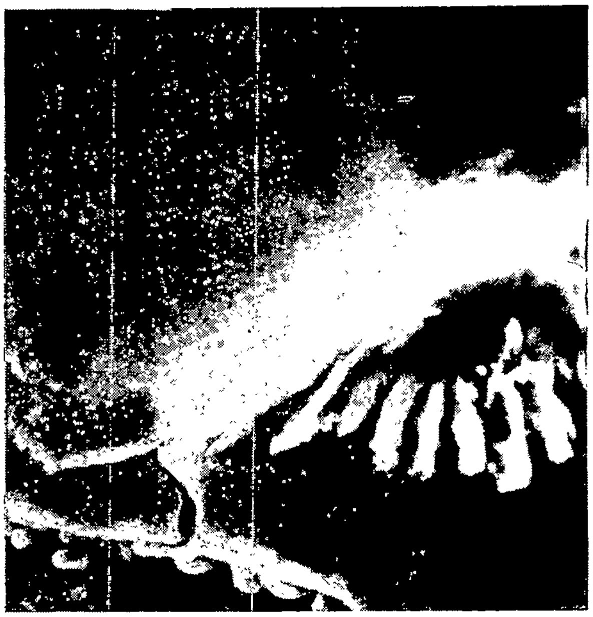

Fig. 1 Tongues of metal and associated spherical particles in the trailing edge of a surface pit, ×2,000.

In the development of the Ferrograph[6] as a diagnostic tool for detecting the rise of abnormal wear conditions in jet engines, it was reported that Ferrograms made from oil taken at intervals from a jet engine, in which the main rolling bearing eventually failed, revealed the presence of lathe-like turnings and spherical particles just before failure. These findings have now been confirmed in many other instances (V. C. Westcott, private communication).

Further investigation of failed balls from accelerated service-simulation rolling contact fatigue tests has confirmed the presence of tongues of metal in the trailing edge of surface pits near the end of the fracture path and spherical particles associated with them (Fig. 1), and revealed evidence

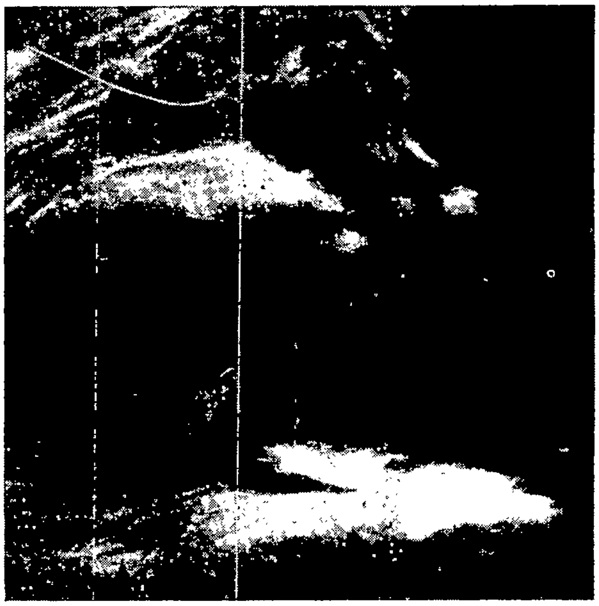

Fig. 2 A detached tongue of metal in process of being worked into a ball in the cavity below an undetached tongue of metal on the fracture surface, ×4,500.

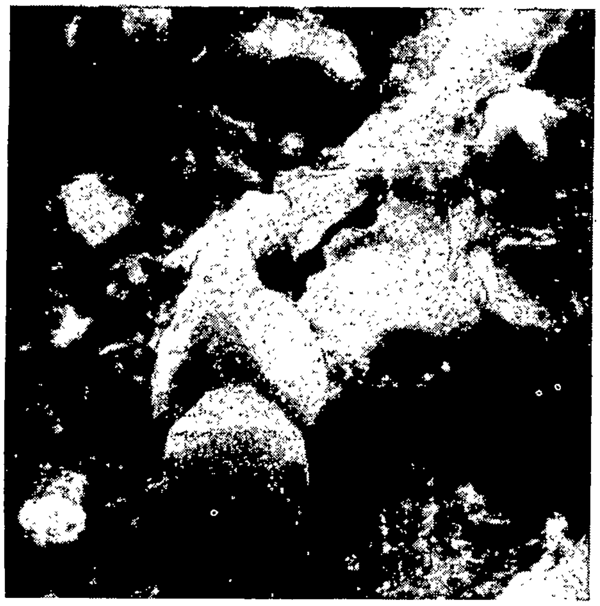

Fig. 3 A spherical particle and a partially formed spherical particle in debris from a jet engine lubricant, × 3,100.

of spherical particles in process of formation by deformation of detached tongues of metal. Fig. 2 shows a detached tongue of metal being rolled into a ball in the cavity below an undetached tongue of metal on the fracture surface.

Ferrograms have also been provided[6] for study. Scanning electron microscopical examination of Ferrograms prepared from the lubricant of a jet engine, which subsequently showed incipient fatigue failure of the main rolling bearing, revealed tongue and spherical particles of debris and evidence of the formation of spheres from the tongues of material. Fig. 3 shows a spherical particle of debris and behind it a spherical particle in process of formation from a tongue of metal. Fig. 4 shows the layer-like structure typical of spherical particles of debris, which is indicative of the mechanism of formation-rolling or balling-up of thin tongues of metal. Analysis of the spherical particles by X-ray energy analysis in the scanning electron microscope and micro-probe analysis confirmed their composition to be that of the material of the rolling bearings.

The presence of spherical particles in lubricating oil, quickly and easily revealed by the Ferrograph and confirmed by electron microscopy and determination of their composition by micro-probe analysis, can form the basis of a powerful diagnostic tool for detection of distress in critical rolling bearing applications and thus prevent catastrophic failure and allow timely maintenance.

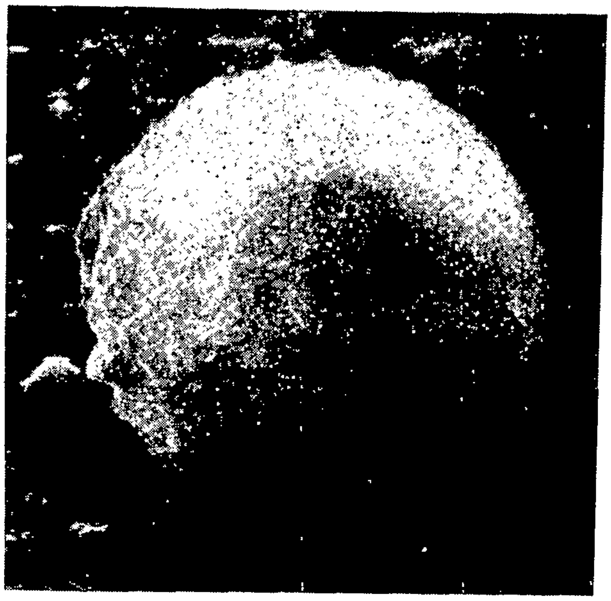

Fig. 4 Typical spherical particle of debris in aero-engine oil showing layer-like structure indicative of formation by rolling or balling-up of material, × 7,000.

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Diamond Synthesis with Non-conventional Catalyst-solvents

THE conventional catalyst-solvents used in the high-pressure, high-temperature synthesis of diamonds from graphite are the group VIII metals, Cr, Mn, Ta, and their alloys[1,2]. A number of other substances have been claimed to act as catalyst-solvents for the graphite-to-diamond reaction, but at the extremely high pressures and high temperatures involved, contamination by the known group VIII catalysts used in the construction of the high-pressure cells may have promoted the diamond-forming reaction. It has been demonstrated experimentally that at sufficiently high static pressures and temperatures graphite will transform spontaneously to diamond[3-6] but the pressures and temperatures are about twice those required for the reactions aided by the conventional catalyst-solvents. Thus substances which may be sub-marginal as catalyst-solvents at the usual diamond synthesis pressures and temperatures might become fairly effective at higher pressures and temperatures[7,8].

Processes have been described which use substances such as Cu, HgO, PbO, and CaO as catalyst-solvents at pressures of 80 to 90 kbar, and temperatures of 1,800 to 2,000° C[9-11], instead of the usual 50 to 55 kbar, 1,300 to 1,500° C. Because earlier experiments had given negative results with Cu, Ag, and Pb at the usual pressures and temperatures, studies of such substances as catalysts at higher pressures and temperatures might resolve the role of a "catalyst-solvent" in promoting the reaction of graphite to diamond.

There are two major theories of the mechanism of diamond formation. First, only the solubility of carbon in a substance determines its efficiency in promoting the graphite-to-diamond reaction. Second, because a number of substances in which carbon is slightly soluble at favourably high temperatures and pressures yield only graphite, and even with conventional catalyst-solvent materials at pressures and temperatures definitely in the "diamond stable region", graphite and diamond crystals can nucleate and grow together, it is suggested that there may be a real difference among carbon solvents in respect of their ability to nucleate diamond; or if a diamond is already present, to nucleate new layers of diamond growth on the diamond surface.

I used a "medium high compression" belt apparatus, capable of 100 kbar pressure, which has been used very successfully for many years; the pressure and temperature characteristics have been well established by a large number of calibration experiments. In the present series all the experiments were run at 85 to 95 kbar pressure. In this apparatus the pressurized region was about 1.25 cm in diameter and 0.80 cm thick.

Two types of cells were used. Fig. 1*a* shows a "directly-heated" arrangement used for the first Cu experiments. The reaction zone consisted of a sandwich of three sheets of Cu with two slabs of spectroscopic rod graphite between them. Heating current was directed to the sandwich by several copper wires at each end, the set of electrode wires at one end going to the top piston and the set at the other end to the bottom piston. The cell was of pyrophyllite. Melting of the copper in the sandwich was indicated quite clearly by a rapid increase in the cell resistance. While the Cu adjacent to the pyrophyllite could be contaminated to some extent by the pyrophyllite, the Cu in the middle was protected by the graphite, giving clean reaction conditions in the hottest part of the cell.

Fig. 1*b* shows the indirectly-heated cell which was designed to have particularly good mechanical and electrical integrity and the best possible chemical cleanliness.

To establish the temperature versus heating power characteristics of the indirectly-heated cell a preliminary experiment was run with a chromel/alumel thermocouple in place in the reaction zone. The pressure correction to chromel/alumel thermocouple readings is known to be negligibly small[12]. Fig. 2 shows the calibration results carried out at pressures of 45 and 82 kbar up to the reliable limit of chromel/alumel—about 1,200° C. The cell materials were stable and clean enough at higher temperatures so that the chromel/alumel calibration could be extrapolated to 2,000° C with reasonable confidence. In test runs with a Pt catalyst the power required confirmed the extrapolation.

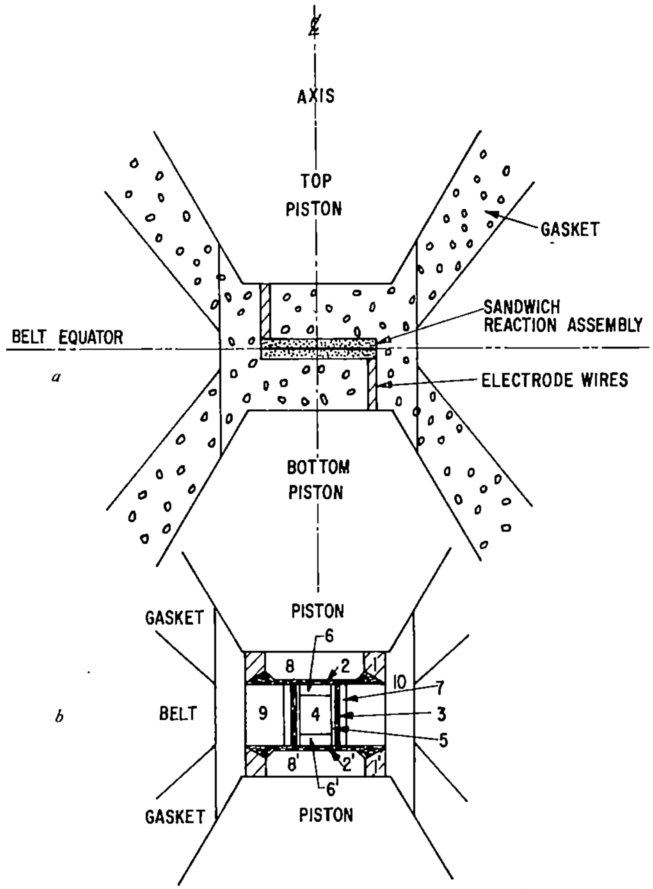

Fig. 1 Cells used in diamond formation experiments. *a*, Section of cell using directly-heated sandwiches of graphite and catalyst metal. *b*, Section of cell with isolated reaction zone (4) indirectly heated by a graphite heater sleeve (3). The heating circuit consisted of the steel current rings 1, 1′, the graphite current disks 2, 2′, and the graphite sleeve heater 3. The reaction zone 4 was inside the graphite heater and isolated from it by the Al_2O_3 sleeve 5 and the Al_2O_3 disks, 6, 6′. The hot zone just outside the graphite heater sleeve was occupied by the Al_2O_3 sleeve 7. The two disks 8, 8′, and the sleeve 9 were made of pyrophyllite stabilized by prebaking in air at about 800° C. The containing sleeve, 10, and the gaskets were of untreated pyrophyllite. Reaction materials were made up in the form of pills of disks and inserted into the space 4. When the reactants were initially powders they were prepressed into right circular pills in a clean pressing mould to bring them to approximately theoretical density before insertion in the high pressure cell. Metal components were punched out as disks from sheets of the desired metal. The reaction chamber, 4, was 0.20 cm diameter by 0.25 cm long. Before test runs parts were stored in a vacuum desiccator at 110° C to minimize absorbed water.

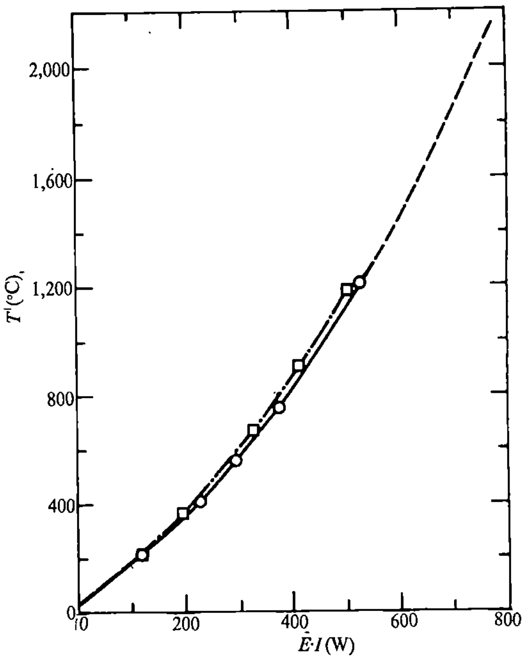

Fig. 2 Temperature/heating power calibration of the cell shown in Fig. 1*b*. □ — · —□, 45 kbar; ○—○, 82 kbar; - - -, extrapolation to 2,000° C.

After runs were made the contents of the reaction zones were examined by optical microscopy, by sapphire scratch testing, and by X-ray diffraction. Operator experience makes such techniques very discriminating.

The first tests on metals were made with the directly-heated cells. The first test was made with Ni which gave the fast, complete, conversion of graphite to diamond expected. Second tests were with Pt, which has a melting point of roughly 2,000° C at the pressure used. Once melted, and reacting, the Pt/graphite cells tended to "run away" in terms of power consumption resulting in overheating and loss of any diamond formed initially. This happened in two runs but subsequent runs, kept under control, gave good diamond yields. Oxygen-free high-conductivity (OFHC) copper was then substituted for Pt and runs were made at the same power levels. The copper melted but gave no reaction at all with the graphite. As a final test of this cell and method, the metal parts were replaced by an alloy of 99 Cu 1 Ni which had been tested at 55 kbar and would not yield diamond[7]. At the higher pressure this alloy formed fine-grained, white diamond rapidly at the areas where melting occurred.

With indirectly-heated cells tests were made using, successively, Pt, PbO, Cu, HgO, CaO, 99 Cu 1 Ni, and 95 Cu 5 Ni at temperatures in the 1,500° C to 2,000° C range. The cells were stable under these conditions. The Pt, 95 Cu 5 Ni, 99 Cu 1 Ni and Cu catalyst-solvents were inserted as disks in the reaction zone, with disks of graphite interspersed between them. Oxide catalysts were used in two ways: (i), powder mixes of the oxides with graphite were prepressed into pills and inserted as such, and (ii), prepressed pills of the oxide and pills of graphite were inserted alternately to form sandwich layers.

The Pt and 95 Cu 5 Ni catalyst experiments yielded diamond readily in this cell, whereas the 99 Cu 1 Ni was marginal with some runs giving small yields and some none. None of the pure Cu runs reacted with the graphite.

The oxide catalyst experiments yielded no diamonds. The oxides of Hg and of Pb decomposed to the metallic element under the conditions of reaction, presumably by carbon reduction of the oxides. In the CaO experiments there was no evidence of reaction. The graphite may have become better graphitized and more slippery as a result of the heating at high pressure in the presence of the CaO.

I conclude that some other conditions—possibly contamination by some other catalytic materials—are necessary to make the graphite–diamond reaction proceed, even at the advanced pressures and temperatures, when Cu, PbO, HgO, or CaO are used as parts of the reaction system.

My experiments using 99 Cu 1 Ni, in which diamond formed, showed that very small additions of conventional catalyst metals are enough to promote diamond formation. The solubility of carbon in this very dilute alloy of Ni in Cu is lower than that in Pb[7]. Because Pb showed no evidence of diamond formation it appears that small amounts of Ni in a Cu alloy, both provide a carbon solvent, and promote diamond nucleation. These higher pressure experiments substantiate the idea that a catalyst-solvent substance for the graphite-to-diamond reaction must be both a carbon solvent and a diamond nucleant.

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BIOLOGICAL SCIENCES

Evolution of Enzyme Regulator Sites: Evidence for Partial Gene Duplication from Amino-acid Sequence of Bovine Glutamate Dehydrogenase

MODULATION of the biological activity of proteins by metabolite levels is a widespread and well-documented phenomenon. As Monod, Wyman and Changeux[1] pointed out, most regulatory protein molecules are composed of several subunits. The regulation of some oligomeric proteins, notably haemoglobin[2], involves interaction of similar sites on separate similar subunits. In other cases such as that of aspartate transcarbamylase[3] there are separate catalytic and regulatory subunits. Some proteins, however, possess within individual subunits both active sites and regulatory sites capable of mediating homotropic and/or heterotropic interaction.

Glutamate dehydrogenase (GDH) from the liver of vertebrates is such a protein. Its catalytic activity is modulated by the coenzymes of the reaction and by such purine nucleotides as ADP and GTP[4-7], and yet the hexameric enzyme molecule contains only one type of polypeptide chain[8]. The precise relation between the purine nucleotide sites and the coenzyme binding sites remains uncertain, but it has been shown clearly that the enzyme can bind more than one molecule of NADH per subunit[4,9-12]. It appears that binding at the second site may account for inhibition by high levels of NADH[13].

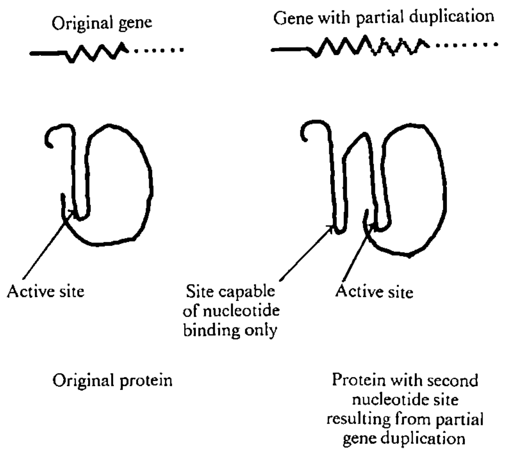
Original gene
Gene with partial duplication
Active site
Site capable of nucleotide binding only
Active site
Original protein
Protein with second nucleotide site resulting from partial gene duplication

Fig. 1 Schematic diagram illustrating the possible partial gene duplication and its consequences in terms of amino-acid sequence, protein structure and enzyme function.

If one assumes that in the course of enzyme evolution catalytic activity preceded the fine control imposed by regulatory sites, the GDH found in vertebrate liver must be descended from an ancestral monomeric dehydrogenase possessing the active but not the regulatory site. It is interesting, therefore, to consider the possible evolutionary origin of the regulatory site.

There are two basic possibilities:

(1) Gradual mutational modification of the genome resulting ultimately in the independent formation of a second, regulatory site, a process analogous to the original evolution of the active site. (2) The incorporation, by unequal crossing-over, for example, of part of a pre-existing gene. In the special case where the regulator is identical with or structurally similar to one of the substrates this would be most simply achieved through partial duplication of the structural gene for the enzyme itself. This would result (Fig. 1) in a protein containing a repeated sequence of amino-acid residues in its molecule.

The disadvantage of the first possibility is its inherently low probability[1]. The second is open to the objection that neither of the duplicated sequences would be in an intramolecular environment identical to that of the ancestral sequence. The protein might therefore fail to fold properly, resulting in obliteration rather than duplication of function. Such a protein would, of course, be discarded by natural selection. Even if the duplicated sequences folded correctly, full function might depend upon participation of other residues which would be accessible to only one of the duplicated sites (Fig. 1). Nevertheless, even if one site retained only a substrate-binding capacity, it could evolve a regulatory function, provided that the other site retained full functional activity. This method offers an evolutionary short-cut and appears more likely than the other.

Although regulatory proteins have not been examined from this standpoint, there are documented cases of duplication having occurred within a single structural gene. Bacterial ferredoxin molecules consist of two clearly related halves[14-17], while those of the heavy chain of gamma G immunoglobulin contain three similar portions[18]. There is also evidence for two gene duplications in the evolution of papain[19].

The nucleotide sequence coding for the potential regulatory site, once established, would mutate independently and probably not conservatively. "Paralogous" sequences as defined by Fitch and Margoliash[20] (human myoglobin and α haemoglobin) tend to diverge more than "orthologous" sequences (human α and β haemoglobins). The duplicated sequences in regulatory proteins envisaged above may be regarded as a special case of paralogous sequences within the

Fig. 2 Comparison of suitably aligned partial sequences of beef liver GDH and pig muscle glyceraldehyde-3-phosphate dehydrogenase. The uppermost of the three sequences shows residues 198–261 of the porcine dehydrogenase. The middle sequence covers residues 267–330 of beef liver GDH, designated the "regulator" sequence in the text. The lower sequence is that of residues 112–175 of the bovine enzyme and includes the active site lysine, Lys 126. The homologies are indicated in capital letters. The GDH sequences are taken from the results of Moon, Piszkiewicz and Smith[21], while the glyceraldehyde-3-phosphate dehydrogenase sequence is that reported by Harris and Perham[23].

G3PDH	GLY	ALA	Ala	Glu	Asn	Ile	Ile	Pro	Ala	SER	Thr	GLY	Ala
GDH2	GLY	ALA	LYS	CYS	Val	Ala	VAL	Gly	Glu	SER	Asp	GLY	Ser
GDH1	Thr	Tyr	LYS	CYS	Ala	Val	VAL	Asp	Val	Pro	Phe	GLY	Gly
G3PDH	ALA	LYS	ALA	Val	Gly	LYS	Val	Ile	PRO	Glu	Leu	Asp	Gly
GDH2	Ile	Trp	Asn	Pro	Asp	Gly	ILE	Asp	PRO	LYS	Glu	Leu	Glu
GDH1	ALA	LYS	ALA	Gly	Val	LYS	ILE	Asn	PRO	LYS	Asn	Tyr	Thr
G3PDH	Lys	Leu	Thr	Gly	Met	Ala	Phe	Arg	Val	Pro	Thr	Pro	Asn
GDH2	ASP	Phe	Lys	LEU	Gln	His	Gly	THR	Ile	Leu	Gly	Phe	Pro
GDH1	ASP	Glu	Asp	LEU	Glu	Lys	Ile	THR	Arg	Arg	Phe	Thr	Met
G3PDH	Val	Ser	Val	Val	Asp	Leu	Thr	Cys	Arg	LEU	GLU	Lys	Pro
GDH2	Lys	Ala	Lys	Ile	Tyr	Glu	Gly	Ser	Ile	LEU	GLU	VAL	ASP
GDH1	Glu	Leu	Ala	Lys	Lys	Gly	Phe	Ile	Gly	Pro	Gly	VAL	ASP
G3PDH	Ala	Lys	Tyr	Asp	Asp	Ile	Lys	Lys	Val	Val	LYS	GLN	
GDH2	Cys	Asp	Ile	Leu	Ile	Pro	Ala	Ala	Ser	GLU	LYS	GLN	
GDH1	Val	Pro	Ala	Pro	Asn	Met	Ser	Thr	Gly	GLU	Arg	Glu	

same protein. In this special case one might expect selective pressures to produce considerable divergences in those parts of the duplicated sequences concerned only with maintaining the structure of the protein.

It was of great interest to search the sequence of bovine liver GDH[8,21] for the vestigial homologies predicted on the basis of the hypothesis above. Two extended sequences in the protein subunit (similar in chicken GDH)[21] show considerable homology. If residues 114–163 are aligned with residues 269–318, no less than 12 of the 50 residues are in identical positions (Fig. 2). The homology includes a Lys-Cys sequence (114, 115) and a Pro-Lys sequence (134, 135) and is greatest in the vicinity of these two sequences. The intervening twelve residues show only one homology. This stretch includes Lys-126 which reacts with pyridoxal phosphate and is thought to be essential for catalytic activity[22]. In the homologous sequence this essential lysine is replaced by tryptophan and there are several other markedly non-conservative changes.

In addition to 24% of their residues in identical positions, the two sequences contain a further 38% that could have resulted from single base changes in the nucleotide sequence.

If one takes two completely random sequences each n residues in length and composed of the twenty common amino-acids, the probability of the occurrence of x and only x homologies is

$$\frac{n!\ 19^{n-x}}{x!\ (n-x)!\ 20^{n}}$$

From this it can be calculated that the probability of 1, 2 or 3 homologies is quite high (0.21, 0.27 and 0.23) but the probability dwindles rapidly for greater numbers of homologies and is 4.3×10^{-6} for 12 homologies. In the GDH sequence, however, there are 352 possible sequences of 50 residues with which to match the sequence in question, if overlapping pairs of sequences are ignored. The probability that one of these sequences will contain 12 homologies with the chosen sequence is therefore $352\times4.3\times10^{-6}$ $(=1.5\times10^{-3})$, as $4.3\times10^{-6}\ll1$. This is an approximation, as no account has been taken of the differing frequencies of different amino-acids.

It seems likely therefore that the homology between residues 114–163 and 269–318 of beef liver GDH reflects common ancestry. Convergent evolution seems most unlikely in this case in view of the marked differences between sequences 119–130 and 274–285. These differences probably reflect the divergence predicted above. Convergent evolution might in any case be expected to produce homologies less mathematically precise and more qualitative in nature.

Smith *et al.*[8] have compared the sequence of bovine GDH with that of glyceraldehyde-3-phosphate dehydrogenase from pig muscle[23], and conclude that there is very little homology, with the exception of the sequence immediately surrounding the active site lysine (Lys 126) of GDH. Residues 209–219 of glyceraldehyde-3-phosphate dehydrogenase and 123–133 of GDH have six residues in identical positions in both sequences. It seemed possible that the "regulator" sequence of GDH might retain homologies with the glyceraldehyde-3-phosphate dehydrogenase sequence that had been lost in the "active site" sequence. Accordingly in Fig. 2 the glyceraldehyde-3-phosphate dehydrogenase sequence is also aligned for comparison. The comparison, summarized in Table 1, shows that outside the region comprising residues 209–219 the glyceraldehyde-3-phosphate dehydrogenase sequence actually shows considerably greater homology with the regulator sequence than with the active site sequence of GDH. Twenty of the 64 residues in the regulator sequence are identical with the corresponding residues in at least one of the other sequences.

Table 1 Comparison of Homology of Glyceraldehyde-3-phosphate Dehydrogenase with "Active Site" and "Regulator" Sequences of Beef Liver GDH

	Identical residues	Alterations explicable by single base changes	Alterations requiring 2 or 3 base changes
G3PDH sequence and matching GDH "active site" sequence	6	30	28
G3PDH sequence and GDH "regulator" sequence	9	21	34
GDH "active" site sequence and GDH "regulator" sequence	12	28	24

The sequences used in this comparison are those shown in Fig. 2.

The evidence for an evolutionary relationship between the three sequences is persuasive. Divergence from an ancestral enzyme probably led separately to glyceraldehyde-3-phosphate dehydrogenase and to a primitive GDH lacking the regulatory site and possessing a subunit considerably smaller than that of beef liver GDH. Later, a partial gene duplication probably resulted in a protein in which a sequence of about 155 residues containing at least part of the active site was repeated. One of the identical sequences must have remained catalytically functional. If the other sequence retained its nucleotide-binding capacity it could then evolve as a regulatory site.

At present no other GDH sequences are available. It is significant, however, that most vertebrate GDHs studied so far are regulated by nucleotides and have molecular weights of about 330,000; the corresponding NADP-linked enzymes from yeast, *E. coli* and *Neurospora* are not regulated by nucleotides and available values for the molecular weights of GDH from lower organisms are all in the region of 250,000[4]. One may predict that when sequences become available for other higher organisms they will further document the partial gene duplication discussed above. The non-regulatory GDH from lower organisms, on the other hand, may well lack the duplicated sequence of 155 residues.

In view of the importance of Lys 126 in the active site sequence and its absence from the corresponding position of the presumed regulator sequence it is most interesting to note that Wallis and Holbrook[24] have shown that the chemical modification of this residue abolishes the binding of 2-oxoglutarate but not the binding of coenzymes. It is likely therefore, as required by the basic hypothesis developed in the present paper, that the replacement of lysine by tryptophan in the corresponding position of the regulator sequence, while abolishing any possible catalytic activity due to that sequence, would leave the nucleotide binding capacity intact.

The present study appears to represent the first evidence bearing upon the evolution of regulatory sites from ancestral catalytic sites. It remains to be seen whether similar mechanisms have operated in the evolution of other regulatory enzymes.

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Mapping the DNA Fragments produced by Cleavage of λ DNA with Endonuclease RI

THE analysis of *in vitro* DNA-directed transcription and coupled transcription/translation is usually complicated by the very large number of products that are made from each DNA molecule. If smaller DNA molecules could be used, the analysis would be correspondingly easier. The discovery of several restriction endonucleases, each recognizing a small number of unique cleavage sites per DNA molecule, could lead to a much deeper analysis of the complex structure and function of DNA by making it possible to isolate homogeneous DNA segments of manageable size. One of these enzymes, the RTF RI endonuclease, has recently been characterized by Yoshimuri, who has shown that it introduces a limited number of cuts in λ DNA[1]; by sucrose gradient sedimentation Yoshimuri separated a faster-moving peak containing one unique DNA population of molecular weight 13×10^6 from a slower-moving peak consisting of smaller fragments of average molecular weight 3.8×10^6. We describe here the further resolution of the products arising from digestion of linear λ DNA with the RI endonuclease into six discrete fragments, and their subsequent characterization and mapping along the λ genome.

When the products of digestion of wild type λ DNA with RI endonuclease are submitted to polyacrylamide gel electrophoresis as described in the legend to Fig. 1, six bands result.

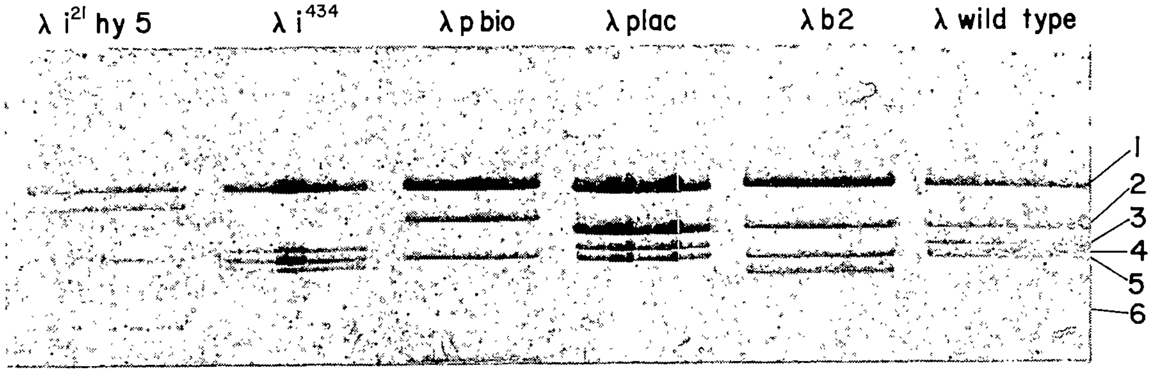

Fig. 1 Polyacrylamide gel separation of the endonuclease RI fragments obtained from various λ DNA species. The phages were grown and the DNA extracted as previously described[2]. The RI endonuclease was purified from an RTF carrying *E. coli* B strain according to Yoshimuri[1], and titrated against λ DNA to determine the amount of enzyme needed to make the reaction go to completion. The DNA was digested with RI endonuclease for 30 min at 37° C in 90 mM Tris-HCl, *p*H 7.5, 10 mM $MgSO_4$. The reaction mixture was then extracted with phenol saturated with 10 mM Tris-HCl, *p*H 8.0, 1 mM EDTA, at 4° C, and the aqueous phase was precipitated with 2 volumes of ethanol at −20° C. The samples (8–15 μg of DNA) were resuspended in 5–10 μl. of electrophoresis buffer (see below) containing 10% sucrose, and 0.02% bromphenol blue as a marker, before being loaded into the sample wells of the gel. The separating gel was a 0.3 cm × 12.5 cm × 12.5 cm slab containing a linear concentration gradient of polyacrylamide, from 2.5% at the origin to a final concentration of 7.5%. (Details of the preparation of the gels will be published elsewhere—P. G. N. J., manuscript in preparation.) The buffer used for the gel and reservoirs was 40 mM Tris acetate, *p*H 8.3, 20 mM sodium acetate, 2 mM EDTA. Electrophoresis was carried out with a current of 45–50 mA for 20 h at room temperature. After the electrophoretic run, the DNA was stained by soaking the gel with a 0.02% solution of methylene blue for approximately 2 h, and then the excess stain was removed by washing the gel with several changes of water. (The methylene blue stained DNA was kept out of strong light to minimize the possibility of photoactivated degradation of the DNA.)

Bands 1, 2 and 3 are well separated. Two other bands run very close together, forming a doublet (bands 4 and 5). The fastest-migrating segment appears to be present in less than stoichiometric amounts (band 6), as indicated by the relatively low intensity of the band seen at this position; the reason for this is discussed below. Each of the bands was eluted from the gel and samples were prepared for electron microscopy length measurements by means of the Kleinschmidt spreading procedure[3,4] (see legend Fig. 2). This permitted an estimation of the molecular weights of the fragments, which are shown in Table 1: the sum of the molecular weights of the fragments agrees closely with the molecular weight estimated for total λ DNA, indicating that together they account for the whole λ DNA molecule. This, in turn, suggests very strongly that each is a unique homogeneous DNA species. Table 1 shows that the distance migrated on the gel is inversely related to the molecular weight determined for each of the fragments, except that 3 and 4, which are well separated by electrophoresis at room temperature (Fig. 1), are found to have identical molecular weights. We have found that if a similar electrophoretic separation is made at 4° C (not shown here) the fragments corresponding to 3 and 4 migrate together. The possible significance of this finding will be discussed below.

As pointed out earlier, fragment 6 is apparently produced in less than stoichiometric amounts. The reason for this became evident from the electron micrographs of DNA extracted from band 1 of the gel (Fig. 2). In some cases there was a small DNA piece, with the same length as a typical segment 6 molecule, lying near the end of the fragment 1 molecule, as if at the last moment the act of spreading for electron-microscopy had separated them. We therefore conclude that fragments 1 and 6 are the two termini of the λ DNA molecule, and that the two frequently migrate together at position 1 in the gel, bound together through the complementary single-stranded regions located at both ends of the total λ DNA molecule[5], thus accounting for the low recovery of pure segment 6 at the faster position on the gel.

The availability of a wide range of well characterized deletion, substitution, and insertion derivatives of phage λ (for an extensive review, see ref. 6) made it possible to compare the gel patterns obtained by digesting wild type λ DNA and some of the derivatives. Fig. 1 shows such an analysis, comparing wild type λ DNA with λ*b*2, λ*plac*5, λ*db*30-7 *nin*5 (which we shall refer to here as λ*pbio*), λ*i*434, and λ*i*21 *hy*5 DNAs. A comparison of the bands present, absent or changed in position for the different mutants with respect to the wild-type pattern, together with the electron microscopy data presented above, allows us to establish the order of the fragments, as shown in Fig. 3.

λ*b*2 is deleted between positions 45.3 and 57.4 of the map (see Davidson and Szybalski[7], and Fig. 3); the band pattern of this mutant lacks fragments 3 and 4 but shows instead a faster-moving piece. This result indicates that fragments 3 and 4 are adjacent, and that the RI recognition site that separates them (and is absent in λ*b*2) is located between map positions 45.3 and 57.4.

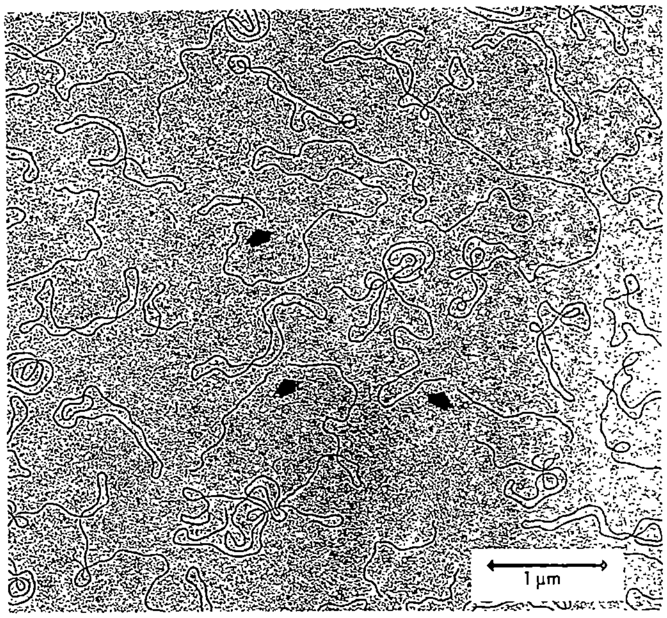

Fig. 2 DNA eluted from position 1 of wild type λ DNA (see Fig. 1) and spread with cytochrome *c* according to the techniques described in Table 1. The arrows point to gaps between short terminal fragments and long terminal fragments of λ DNA, which were pulled apart during the spreading with cytochrome *c*.

λ*pbio* has been studied extensively by Fiandt *et al.*[8] and contains two alterations of the wild type λ genome: (1) the DNA between map positions 56.5 and 77.5 has been deleted, and instead some genes of the *bio* operon have been inserted, corresponding to 9.3 λ units in length; (2) a further deletion occurs between map positions 83.8 and 89.2. The band pattern for this mutant shows that wild-type DNA segments 2, 3 and 5 have been replaced by a slow-migrating band between wild-type fragments 1 and 2, and a band migrating faster than wild-type fragment 5. Hence it can be deduced that, as fragment 4 appears unaltered in the gel pattern, the RI recognition site between wild-type segments 3 and 4 must lie outside the 56.5–77.5 λ*pbio* deletion, and this site must be to the right of segment 4; furthermore, both segment 2 and segment 5 must lie to the right of segment 3.

The single remaining piece of evidence necessary to complete the ordering of the fragments comes from the band pattern obtained with λ*i*434. This mutant differs from wild type λ in its immunity region, which is smaller than and mainly nonhomologous to the λ immunity region[8]. As the fragment corresponding to wild type segment 2 is the only one missing from this mutant, being replaced by a fragment migrating just below fragment 5, the immunity region must

Table 1 Molecular Weight Determination of the Fragments

	Total λ	Fragment No. 1	2	3	4	5	6
No. of molecules measured	16	13	16	28	28	22	30
Average lengths (μm)	16.80	7.79	2.68	2.11	2.07	1.75	1.26
Standard deviation (μm)	±0.36	±0.24	±0.092	±0.051	±0.042	±0.049	±0.027
MW * × 10^6	30.85	13.69	4.49	3.54	3.54	3.00	2.31

* Calculated by comparison with PM2 DNA (molecular weight = $6.40 \times 10^6 \pm 2\%$) used as internal standard.

Bands of wild type DNA fragments, separated as shown in Fig. 1, were cut out from the gel (fragments 4 and 5 were taken together). The gel pieces were transferred into plastic tubing, and their DNA content was collected electrophoretically into dialysis tubing immersed in the lower reservoir of the electrophoresis apparatus (12 h at room temperature, 50–100 V). The buffer for this elution was the same as that described in Fig. 1. The DNA was then concentrated by ethanol precipitation followed by resuspension in 10 mM Tris, *p*H 8, 1 mM EDTA. The spreading of the DNA with cytochrome c and 30% formamide was done as described earlier[3,4].

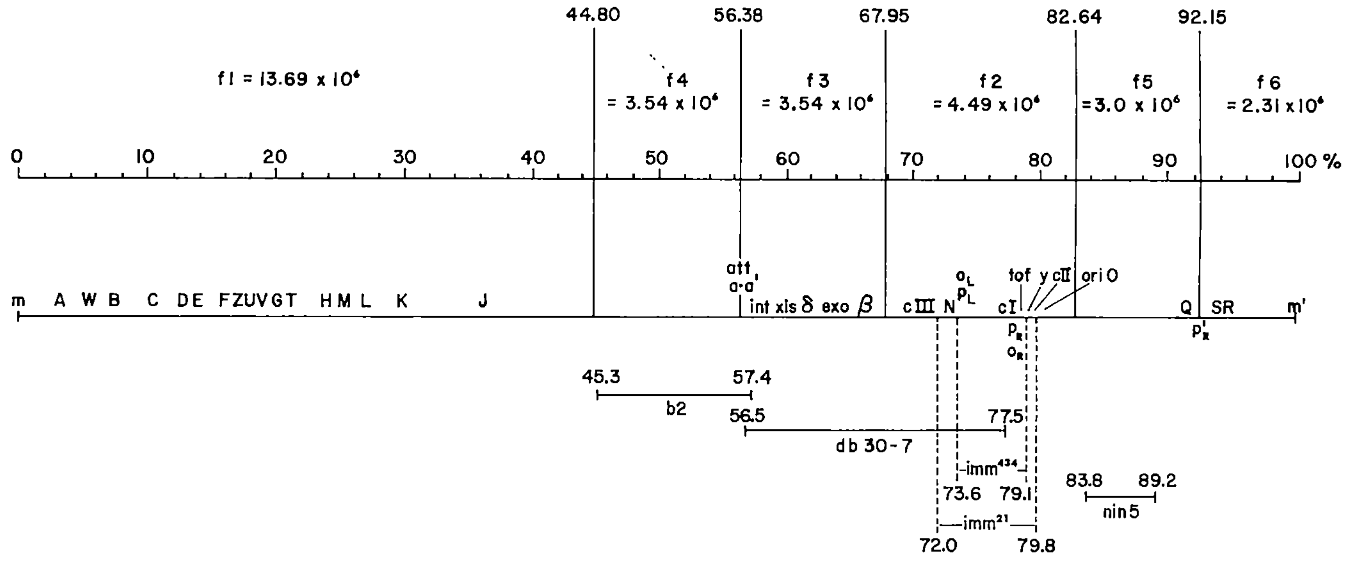

Fig. 3 Position of the six λ DNA fragments along the whole molecule. The positions of the RI endonuclease cleavage sites, as established by combined electron microscopy and gel analysis data, are indicated on the λ DNA map (adapted from Davidson and Szybalski[7], with permission). We assume that the total ÷ scale represents the sum of the molecular weights found for the six fragments, that is, 30.57×10^6 daltons. This value agrees closely with that estimated by Davidson and Szybalski[7] ($30.8 \pm 1 \times 10^6$), and also with our measurement of the total λ DNA (30.85×10^6) (Table 1).

be located in segment 2. There is also a new, very fast-migrating band in the λ*i*434 pattern, probably arising from a further RI recognition site within the λ*i*434 nonhomologous immunity region.

The electron microscopy data combined with the mutant analysis lead to the order of fragments shown in Fig. 3. Molecular weight considerations dictate that segment 1 is the left-hand terminus and segment 6 the right-hand terminus of the λ DNA molecule. The two remaining mutants analysed in Fig. 1 lend confirmation to this order of fragments. Thus λ*plac*5 contains an insertion of the genes of the *lac* operon in a region previously located somewhere between genes J and N[9]; in λ*plac*5, fragment 4 is replaced by a larger DNA segment migrating very close to wild type fragment 2. From Fig. 3 we can therefore locate the position of the *plac*5 insertion between map positions 44.80 and 56.38, which are indeed between genes J and N (see Fig. 3).

The hybrid λ*i*21 *hy*5 is known to contain the phage 21 immunity region and, in addition, further uncharacterized regions of nonhomology with wild-type λ. Its pattern of cleavage by the RI endonuclease suggests that it lacks the wild-type enzyme recognition sites between segments 2 and 3, and between segments 3 and 4. As a result, the hybrid possesses a large fragment migrating just faster than wild type fragment 1. The λ*i*21 band pattern also shows a DNA fragment of lower molecular weight than wild type fragment 6, suggesting that either (1) the corresponding region of DNA in the hybrid is smaller than in wild type λ, or (2) the RI enzyme recognizes a new site in the λ*i*21 immunity region. In the latter case, the absence of segment 6 from the gel pattern of the hybrid would be due to a complete adhesion of the two termini during the gel fractionation procedure. We have not investigated these possibilities further.

It should be noted that in the above argument we have assumed that if a DNA fragment from a mutant co-migrates on the polyacrylamide gel with a fragment of wild type λ DNA, then the two fragments are, except for possible minor sequence differences, identical and come from the same region of whole λ DNA. The internal consistency of the results obtained and their agreement with the known physical map of the λ DNAs employed strongly suggest that this assumption is correct.

These results show that it is possible to separate DNA fragments of molecular weights up to approximately 5×10^6 according to their size by polyacrylamide gel electrophoresis. As the molecular weight increases, however, such separations become more difficult in this system, and DNA fragments of greater than approximately 10^7 molecular weight tend to move together in a very close band in the position of fragment 1 (unpublished observation). Moreover, at room temperature, smaller size DNA pieces may also exhibit unexpected mobilities; fragment 4, which shows a greater mobility at higher temperatures with relation to the other fragments, lies mainly in the *b*2 region of λ DNA, which has been shown to be low in G+C content (37%)[6]. Perhaps by virtue of this base composition, increasing temperatures render fragment 4 less rigid, and hence less resistance is offered to its motion through the gel at room temperature.

Our ability to separate the fragments produced by digestion of λ DNA by the RTF RI endonuclease simply on polyacrylamide gels, and to establish their location on the λ genome, should make it possible to characterize any strain of λ phage in which large deletions, substitutions, or insertions occur in the DNA, as illustrated above in the cases of λ*plac*5 and λ*i*21. Furthermore, the availability of homogeneous segment preparations of known regions of the whole λ DNA, such as we have described, should facilitate studies on *in vitro* transcription, coupled transcription/translation, and sequence analysis of λ DNA.

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Magnetic Resonance Studies of Deoxyribonucleoprotein

THE structure of chromatin, and the problems of organizing large lengths of DNA within the cell nucleus, are currently of considerable interest. It now appears established that the agents of chromosome structure are the histones found in conjunction with DNA in the chromosome, which may also act at some stage of genetic regulation. Of the five major types of histone fraction normally associated with mammalian genetic material, the lysine-rich histone F1 (or histone I) has some properties which set it apart from the others. It contains a very high proportion of lysine (27%), alanine (24%) and proline (9%) residues, these three alone making up more than 60% of the 216 residues of the molecule. As expected from the high proline content, F1 forms very little α-helix[1] in aqueous salt solutions; it also shows less tendency to aggregate than the other fractions. Interchain interactions, however, involving a specific section of the molecule are induced by salt[2,3]; a proposed scheme for this interaction, involving an antiparallel alignment of chain segments, has been presented[3].

Another distinguishing feature of F1 is the relative ease with which it is removed from the deoxyribonucleoprotein complex. It is completely removed by 0.4–0.5 M NaCl[4] or by 0.1 M MgCl[5] while all the other fractions remain bound to the complex, though not necessarily to the same sites[6] at these molarities. This ready removal of F1 from an otherwise stable complex forms the basis of the N.M.R. studies to be described.

Several roles have been suggested for F1. Mirsky *et al.*[7] have shown by electron microscopy that F1 is associated with a "clumping" of DNA fibres. Ord and Stocken[8] have produced evidence that the phosphorylation of histones may modify their interactions with DNA, and Bradbury, Inglis, Matthews and Sarner (unpublished results) have shown that the lysine-rich histone fraction in *Physarum polycephalum* is phosphorylated just before mitosis, at a time when chromosome condensation is taking place. These and other results suggest that the lysine-rich histone fraction found in DNP may play a large part in the high-level organization of chromatin and perhaps in the condensation of the chromosome, which is supported by our present results.

Nuclear magnetic resonance spectra were obtained, using a standard time-averaging computer, on the 'Jeol JNM-4H' 100 MHz spectrometer and on the 'Varian HR-220' spectrometer belonging to the SRC. Standard 5 mm tubes were used. No attempt has been made at this stage to compensate for changes in sample concentration consequent upon gel condensation. Simulated spectra were generated as described[8]. DNP was prepared by the method of Zubay and Doty[10]. The final gel was analysed by infrared spectroscopy[11] and always showed between 52% and 56% of protein in the complex. Partial DNP ($P_{0.6}$) was obtained by homogenizing DNP gel with 40 volumes of 0.6 M sodium chloride, stirring for 2 h, and then pelleting at 140,000*g* for 3 h. Subsequent analysis of the histones in this material by the polyacrylamide gel electrophoresis technique of Johns[12] showed that 6–8% of the original F1 content remained. A more completely F1-depleted material ($P_{0.6\ +\ CMC}$) was obtained by adding carboxymethyl cellulose to the DNP homogenate at the stirring stage; the resulting partial DNP contained less than 2% of the original F1 as estimated from densitometer traces. Photographs of the polyacrylamide gels obtained from the DNP and the F1-depleted DNP are shown in Fig. 1 (*g*) and (*h*).

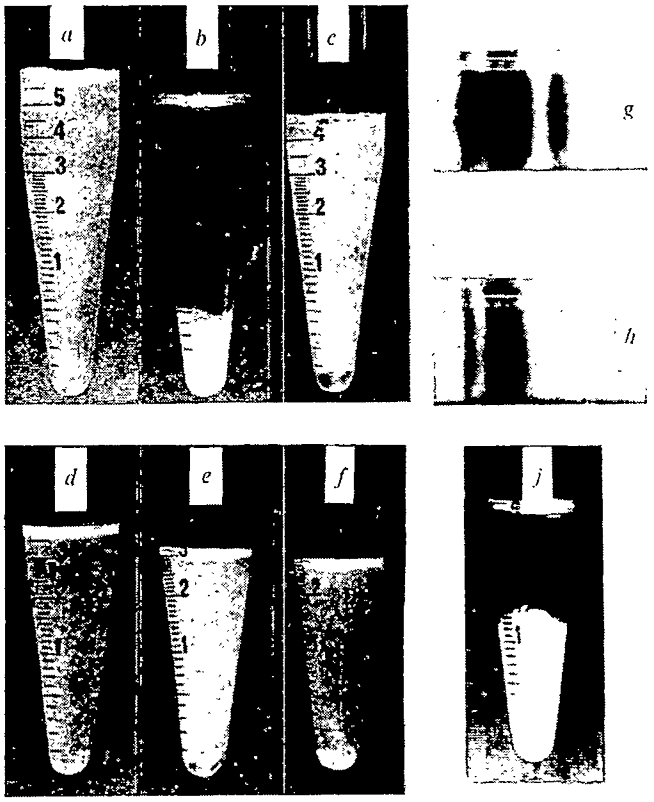

Fig. 1 Deoxyribonucleoprotein gel after spinning at 1,000*g* for 5 min. *a*, Total DNP in D_2O; *b*, Total DNP in 0.2 M NaCl; *c*, Total DNP in 0.5 M NaCl; *d*, Partial DNP ($P_{0.6+CMC}$) in D_2O; *e*, Partial DNP in 0.2 M NaCl; *f*, Partial DNP in 0.5 M NaCl; *j*, DNP gel containing ~7% of original histone F1, in 0.2 M NaCl; *g*, Polyacrylamide gel pattern of histones from total DNP; *h*, Polyacrylamide gel pattern of histones from partial DNP ($P_{0.6+CMC}$).

When the ionic strength (NaCl) of a DNP gel is increased a reversible contraction occurs (Fig. 1, *a*, *b*, *c*). These photographs are all of the same sample; in each case the sample has been dialysed overnight against 500 volumes of the stated sodium chloride solution, transferred to a centrifuge tube and spun at 1,000*g* for 5 min before being photographed. It can clearly be seen that at an ionic strength of 0.2 M NaCl, the gel has shrunk to about one-tenth of its original volume (Fig. 1*b*) while an increase to 0.5 M NaCl causes a complete return to the original volume (Fig. 1 *c*). No such shrinkage takes place in gels from which F1 has been removed (Fig. 1, *d*, *e*, *f*). Further, the partial nucleoprotein $P_{0.6}$ containing 6–8% of its original F1 shrinks to about 35% of its original volume (Fig. 1 *j*). A quantitative estimate of the shrinkage caused in total DNP by NaCl and by $MgCl_2$ is given in Table 1.

Gel shrinkage corresponds to a solubility minimum noted by several workers[13]. We have measured the turbidity of solutions of total and F1-depleted DNP by monitoring the absorbance at 600 nm, and find that a very large increase in turbidity is shown by total DNP over the range 0.1–0.3

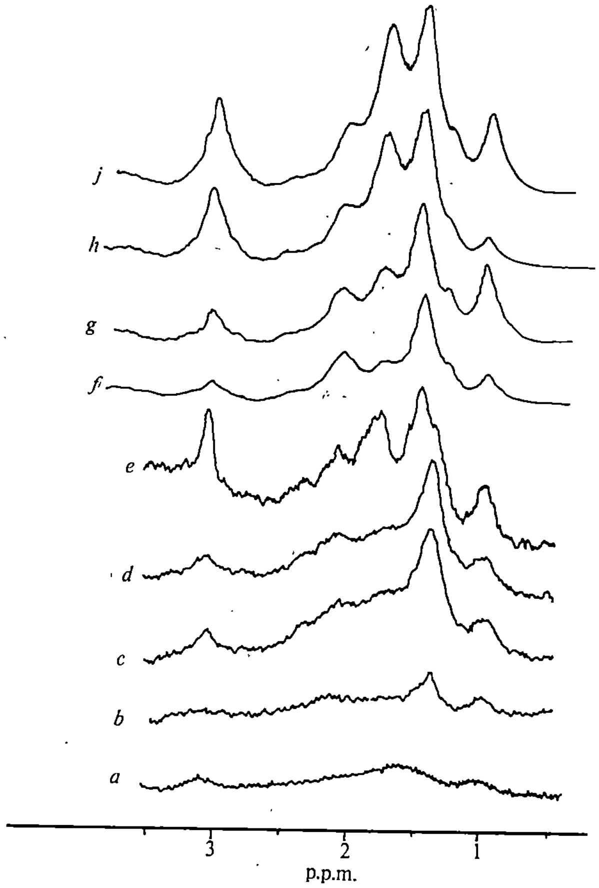

Fig. 2 High-field parts of (*a*). 100 MHz NMR spectrum of F1-depleted DNP; and 220 MHz spectra of total DNP in (*b*) D_2O, (*c*) 0.1 M NaCl, (*d*) 0.25 M NaCl and (*e*) 0.5 M NaCl; simulated 220 MHz spectra of histone fraction F1, (*j*) in random-coil form, (*h*) with signals from residues 47–106 broadened, (*f*) and (*g*) as (*h*) and (*j*) but with the resonances of 40 lysine residues removed.

M NaCl. No corresponding change in turbidity is shown by F1-depleted DNP (Fig. 5).

Detailed studies[3] have clearly shown that in 0.5 M NaCl the NMR spectrum of F1 indicates a motion-reducing interaction involving only the section of the molecule between residues 47 and 106. This section comprises 27% of the whole molecule, but contains 75% of the apolar (Val, Leu, Ile) residues and only 14% of the total lysine residues. A model for the interaction can be formulated, based on a linear association of antiparallel molecules (Fig. 7 of ref. 3).

The 220 MHz spectra of DNP gel in the presence of varying concentrations of sodium chloride are shown in Fig. 2 *b–e*. The almost complete absence of signal in 2 *b* indicates that in the non-condensed gel in D_2O, the molecular structure is very rigid so that the spectrum is unobservably broad. Changing the ionic strength to 0.1 M NaCl (2 *c*) causes the appearance of peaks whose chemical shifts correspond mainly to those of alanine, proline and lysine residues, accompanied by gel condensation. Neither the spectrum nor the condensation is found in DNP whose F1 has been removed (Fig. 2 *a*). Further increase to 0.25 M NaCl (3 *d*) causes no observable change in either the condensation or the NMR spectrum, but upon reaching 0.5 M NaCl, which produces re-expansion of the gel and corresponds to the removal of F1 from the complex, new peaks appear in the spectrum 2 *e*. These have the chemical shift of lysine resonances; and the resultant spectrum is identical with that of free F1 in 0.5 M NaCl, the only difference being that all the lines are broader by a factor of about 1.8. The greater linewidth found in the gel is ascribed to an increased viscosity effect within the gel structure.

Table 1 Shrinkage of Nucleoprotein Gel *

Medium	Contracted volume as percentage of initial value		
Sodium chloride	0.1 M 18%	0.25 M 13%	0.6 M No observable shrinkage
Magnesium chloride	0.0005 M 12%	0.1 M 64%	
Urea	6.0 M 24% expansion		

* Initial concentration of DNA in gel 6.25 mg ml.$^{-1}$.

A set of computer-generated model spectra are included in Fig. 2 for comparison. Fig. 2 *j* is the simulated spectrum of F1 in D_2O, and Fig. 2 *h* represents the spectrum obtained when the segment from residues 47 to 106 is assumed broadened by interaction. 2 *g* and 2 *f* are as 2 *j* and 2 *h* but with the added assumption that the signals of 40 of the 60 lysines of the molecule are broadened by interaction. These F1 spectra with lysine resonances removed correspond closely to those obtained from DNP in its contracted state. We therefore draw the following conclusions from the spectra of Fig. 2:

(a) In the salt conditions used, no spectrum appears which is not directly attributable to the molecules of F1 in the complex. No spectrum appears in samples from which F1 has been removed. This implies that up to 0.5 M NaCl, all the other components of the system, the other histone fractions, other proteins, and DNA, form a complex which is too rigid to give a high-resolution NMR spectrum. It may also be assumed that the spectrum of parts of F1 only becomes visible when those parts are not bound to the rigid complex. (b) Under conditions of low ionic strength, where there is no gel condensation, all the histone F1 is firmly bound to the complex. (c) Under conlitions corresponding to gel condensation, most of the lysines of histone F1 remain firmly bound, and the spectrum which appears

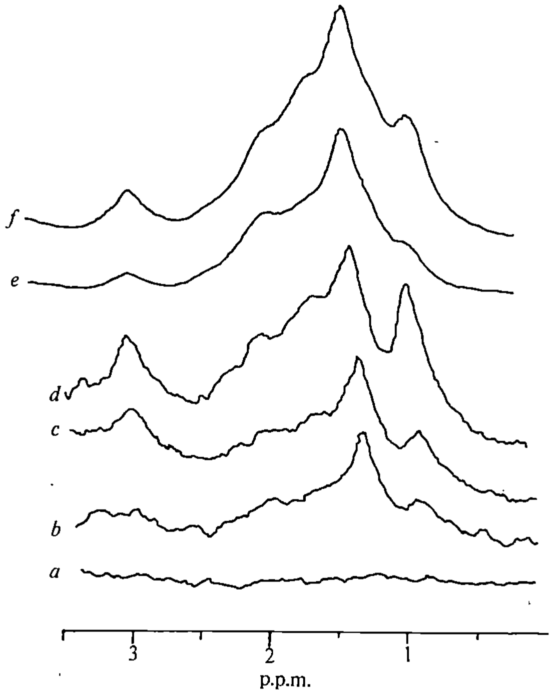

Fig. 3 High-field parts of 100 MHz n.m.r. spectra of total calf thymus DNP in (*a*) D_2O; (*b*) 0.5 M urea-d_6; (*c*) 3 M urea-d_6; (*d*) 6 M urea-d_6. Simulated spectra of histone fraction F1 with 40 lysine resonances removed; (*e*) with signals from residues 47–106 broadened and (*f*) in the random coil form.

is otherwise that of F1 molecules in which an interaction is taking place between segments 47–106 (compare spectra 2 *c* and 2 *f*). (d) Complete removal of the histone F1 results in re-expansion of the gel and a freeing of the lysine residues from the complex. The spectrum obtained is that of F1 with segments 47–106 interacted.

Fig. 3 shows the changes induced in the 100 MHz spectrum of DNP by dialysis against urea, and some simulated spectra drawn from the same data as Fig. 2 *f* and *g* but corrected to 100 MHz. The following points may be made about these spectra ; (a) Even at 6 M urea, not all the expected lysine resonances have appeared, indicating that the F1 is still partly bound to the complex. As lysine residues would be expected to form ionic linkages, this is perhaps not surprising. (b) The peak at approximately 1 p.p.m., arising from sidechain CH_3 resonances of apolar residues, is very pronounced in 6 M urea solution, indicating that these residues, which form a major part of the interacting segment 47–106 of the F1, are very free moving and not involved in any interaction. This is very interesting in view of the fact that urea does not cause a contraction, but rather an expansion, of the gel. Urea tends to destroy hydrogen bonds and hydrophobic interactions, having far less effect on ionic linkages. Thus while there is strong evidence that histone F1 is bound to the DNP complex by ionic linkages through its many lysine residues, it also appears that active condensation cannot take place under conditions unfavourable to hydrogen bonds and hydrophobic interactions; interactions of these types are the most numerous in the proposed antiparallel F1-F1 interactions.

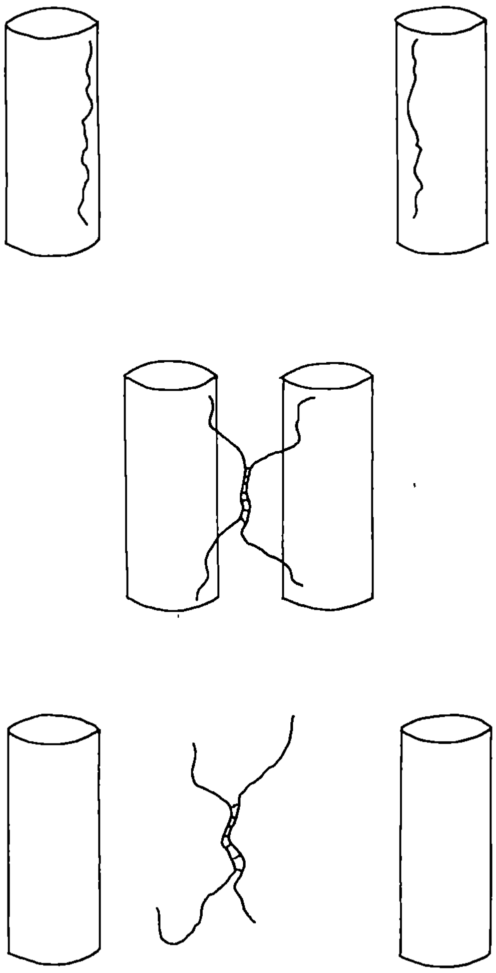

Fig. 4 Proposed mechanism for shrinkage of DNP gel. The cylinders represent all of the DNP except F1, the single lines F1 molecules. *a*, In H_2O, with gel expanded and F1 bound to the rest of the complex. *b*, In 0.1–0.3 M NaCl, region 76–106 of F1 freed from complex. F1–F1 antiparallel interactions cause gel shrinkage, as lysine-rich ends of F1 are still bound to the complex. *c*, In 0.5 M NaCl. The F1 is now freed completely from the complex, leaving it free to expand to its original volume.

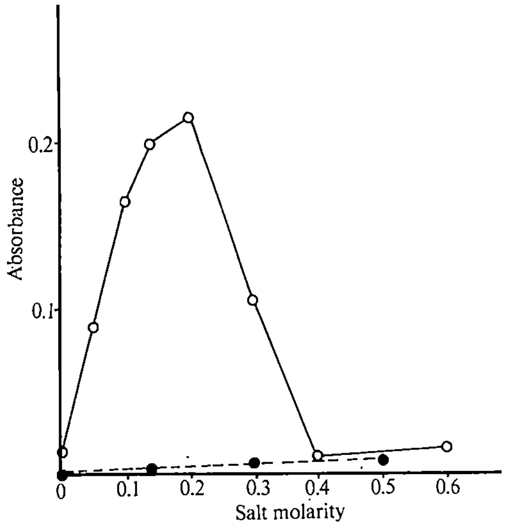

Fig. 5 Turbidities of total (DNP) and F1-depleted ($P_{0.6+\mathrm{CMC}}$) DNP showing variation with NACl concentration. ○—○, DNP; ● - - - ●, Partial DNP (F1 depleted). Turbidities measured at 600 nm, 10 mm path length cells.

We conclude from our results that the lysine-rich histone F1 is necessary to the condensation of calf thymus DNP, and that F1 is bound by its lysine residues, which are mostly located at the amino end and in the carboxyl half of the molecule, to the rest of the DNP complex. The rest of the complex has a rigid structure which it maintains even under conditions which completely remove the F1. Condensation of the gel is associated with the freeing of large parts of F1 from the complex, while retaining some binding *via* the lysine residues, and the subsequent setting up of an interaction between F1 molecules which involves the segments from residues 47–106. The breaking of the ionic bonds holding the F1 to the rest of the complex coincides with complete re-expansion of the gel. A proposed mechanism for the contraction of DNP gel incorporating these conclusions is given in Fig. 4.

There have been several suggestions that modifications of histones are involved in controlling the physical state of chromatin[14]. Langan[15] has clearly demonstrated the phosphorylation of serine residues in rat liver F1 and suggested that such modifications might change the F1-DNA interactions. In this respect Cole (private communication) has suggested that phosphorylation of the serines (37 and 106) at each end of the interacting segment may control changes in the interactions of the central segments. This, together with the observations that phosphorylation of the very lysine-rich histone occurs at the time of chromosome condensation, leads to the interesting speculation that phosphorylation, rather than changes in ionic strength, may serve as the trigger to condensation processes similar to those described above in living systems.

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Nuclear DNA Contents of Coelacanth Erythrocytes

AMONG the living fishes, groups of widely different phylogenetic antiquity may be classified by equally diverse sets of characteristics, both morphometric and biochemical. One such character that has been used in the study of the relationships between the major groups is cellular DNA content. It is now well known that, among fishes, modern teleosts have the lowest diploid levels (as low as 0.8 pg) and that elasmobranchs have somewhat intermediate levels (3–15 pg). The Dipnoi have the highest levels among living vertebrates (160–285 pg), and these values are approached most closely by some (but by no means all) Amphibia, such as *Necturus* and *Amphiuma* (205 and 192 pg respectively)[1,2].

Table 1 DNA-Feulgen Content of Erythrocyte Nuclei

Species	Number of nuclei measured	Mean Feulgen dye content in arbitrary photometric units ±error of the mean	DNA content per diploid genome ($g \times 10^{-12}$)
Xenopus laevis	10	47.5±2.2	6.3
Rana pipiens	10	115.7±2.8	15.3
Latimeria chalumnae	20	99.7±1.7	13.2

Fresh blood was smeared on microscope slides and allowed to dry. Slides from all three species were fixed and stained as a single batch. The preparations were post-fixed in ethanol-acetic acid (3:1) for 3 min, hydrated, hydrolysed in 5 N HCl for 1 h at 25° C and stained for 1 h with the Feulgen reagent. Dye contents of individual nuclei were measured by the two wavelength method of microspectrophotometry (λ^1=560 nm; λ^2=487 nm). The relative dye contents are given in arbitrary photometric units. The absolute DNA contents for *Rana* and *Latimeria* were estimated on an assumed value of 6.3 pg per diploid genome for *Xenopus*[5]. The estimated value for *Rana* agreed with literature values[6].

In view of this great diversity of nuclear DNA content in fishes, and indeed all vertebrates, it has not always been clear what level might be considered "primitive" and what "advanced"[3]. It would therefore be extremely interesting to know the nuclear DNA content of supposedly primitive organisms. We have studied blood samples of a live coelacanth *Latimeria chalumnae* Smith, captured by a recent American-British-French expedition to the Comore Islands[4]. Cytophotometric measurements of Feulgen-stained erythrocyte nuclei show that the DNA content of *Latimeria* erythrocyte nuclei is 13.2 pg (Table 1). (This confirms predictions about histological thin sections of coelacanth tissues[2,7].) Coelacanths therefore have diploid DNA levels well above some Amphibia, such as *Xenopus* (6.3 pg per diploid cell[5]) and in the same range as *Rana* (15.3 pg, Table 1) and elasmobranch fishes such as *Squalus acanthias*[2] (14.7 pg).

The DNA content in *Latimeria* was higher than would be expected in the ancestor of all tetrapods and we conclude that in the course of evolution from the original dipnoan-crossopterygian-amphibian stock, increase in the coelacanth genome has occurred. Thus increased cellular DNA contents have arisen many times, independently, in this whole assemblage.

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Trans-β-farnesene, Alarm Pheromone of the Green Peach Aphid, *Myzus persicae* (Sulzer)

THE chemical structure of the repellent odour found in the cornicle secretion of the aphid *M. persicae*[1] has been identified as trans-β-farnesene.

We used two different methods to obtain material for gas chromatographic and mass spectrum analysis. In the first, a stream of dry nitrogen was passed over a homogenate of 0.6 g of aphids into a cold trap (−60° C). The collected material, dissolved in pentane, gave a positive bioassay by repelling other *M. persicae* on a radish plant. Gas chromatography (g.c.) at 115° C on an 'OV-17' column gave a single peak eluting at 7.5 min. After elution of this peak a 3° min^{-1} programme to 190° C caused the elution of a large number of peaks beginning at 175° C. A g.c. mass spectrum of the 7.5 min peak gave a molecular ion of 204 $m\ e^{-1}$ and three prominent ions in decreasing order of 69, 93, and 41 $m\ e^{-1}$. Other characteristic ions were 120, 133, 161, and 189 $m\ e^{-1}$.

A second sample was prepared by soaking 2 ml. of *M. persicae* in 2 ml. of refrigerated pentane for 5 days, as separate observations showed that pentane caused cornicles to open and expel fluid. A single peak eluting at 6.5 min from a 4 foot, 15% stabilized 'DEGS' column at 100° C was passed over *M. persicae* feeding on radish. The aphids responded by withdrawal of stylets from the leaf and by walking from the leaf. An aliquot (1/10) of the extract was purified by cold-trapping the 6.5 min peak from this column, and this also gave a positive bioassay. The hydrocarbon nature of the compound was verified by co-chromatography with C_{16} and C_{14} saturated hydrocarbons on a 6 foot 'UC-W98' (10%) column at 150° C. The active peak eluted shortly after C_{14} and by interpolation of elution times had a boiling point of 258° C. A g.c.-mass spectrum of the active peak prepared in this manner also gave a molecular ion of 204 $m\ e^{-1}$ with prominent ions of 69, 93, and 41 $m\ e^{-1}$ and the characteristic ions 120, 133, 161 and 189 $m\ e^{-1}$.

The mass spectra in both instances were nearly identical to that reported for trans-β-farnesene[2]. Synthesis and mass spectroscopy of trans-β-farnesene revealed that this compound and the aphid odour were identical. Bioassay of trans-β-farnesene was carried out by crushing a sealed glass ampoule containing approximately 10 mg of synthetic trans-β-farnesene in the presence of *M. persicae* on turnip leaves. A large number responded by falling or walking from the plant.

Combined with insecticidal sprays for the control of aphids, the alarm pheromone could enhance their effectiveness. The pheromone will cause those aphids avoiding a direct hit by a spray droplet to walk over the plant and contact the insecticide.

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Note added in proof. At the time this manuscript was submitted for publication Dr W. S. Bowers, USDA, Beltsville, Maryland, informed us that he had established that trans-β-farnesene was also the alarm pheromone for the rose aphid, *Macrosiphum rosae.*

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Transplantation of Killer Endosymbionts in Paramecium

Several syngens or breeding groups of *Paramecium aurelia* contain endosymbionts which may result in the development of the killer trait[1]. The symbionts are of different morphological types and it has been suggested that these are non-randomly distributed between syngens[2]. Experiments involving crosses between paramecia with and without symbionts showed that each endosymbiont required a specific nuclear gene for its maintenance. A single gene controlled the presence or absence of endosymbionts as shown by segregation in the F_2 generation. The pattern of loss of symbionts in some of those F_2 clones varies, generally extending over a number of asexual fissions which for different endosymbionts can be from two to over sixty. Infection experiments also demonstrate the requirement for a specific gene. Infection of endosymbionts from homogenates or purified preparations occurs *via* the medium but only into particular cells possessing a specific gene[1,3]. Finally, some endosymbionts growing *in vitro* retain their infectivity into certain paramecia (author's laboratory).

As intersyngenic matings generally do not produce viable progeny, it has not been possible to test for the presence of the maintenance gene in different syngens. Also infection of symbionts from the growth medium back into the source paramecia is not always possible. We tried to transfer endosymbionts between syngens by microinjection. Such intersyngenic transfer, of kappa endosymbionts between syngen 2 and 4 have been recorded[4]. Experiments of this sort may tell us about the distribution of the maintenance genes within the syngens of paramecia, thereby indicating genetical and geographical relationships between symbionts and host paramecia.

Paramecia were grown in grass medium. The transplantation or microinjection technique involves transferring cytoplasmic material from one cell to another with a Fonbrunne micromanipulator (ref. 4 and J. Knowles, personal communication). The presence of endosymbionts was scored by the method of Beale and Jurand[5] or by squashing cells and examining exudates under the phase contrast microscope.

Table 1 Successful Transfer of Symbionts

Symbiont injected†	Recipient cells* which accept symbionts			
1(540) mu‡	1–540(25)§	1–551(39)	1–90(18)	8–138(14)
2(7) kappa	2–7(23)	2–511(54)	4–51(7)	
2(562) alpha	2–562(31)	2–511(18)		
4(51) kappa	4–51(28)	4–116(22)	2–7(3)	
4(A_1) kappa	4–A_1(15)	4–51(23)		
8(138) mu	8–138(21)	8–131(26)	1–540(5)	
8(299) lambda	8–299(8)	8–131(18)		

* None had symbionts.

† Symbionts isolated from packed cells. Paramecia were resuspended in 3 volumes of buffer (0.25 M sucrose, 100 mg ml.$^{-1}$ bovine serum albumin, 0.001 M potassium phosphate, pH=7.0) at 4° C and homogenized in a 'Waring' blender. After centrifugation at 2,000*g* for 20 min the supernatant contained the symbionts —mu 540, mu 138 [6], alpha 562 and kappa (A_1), (51)[3,7] and lambda 299[8].

‡ Numbers refer to the stock and syngen of *Paramecium*, for example, 1(540) is stock 540 of syngen 1.

§ Actual number of cells injected successfully. Where the symbionts could be injected 100% success was achieved.

Symbionts (kappa, mu, alpha, lambda) were prepared from mass cultures of cells[3,6–8], and transferred to other paramecia. At least twenty cells were injected in each experiment and there was at least 50% survival. The results of various intrasyngenic and intersyngenic transfers of symbionts are shown in Table 1.

Each endosymbiont can be successfully injected into at least one other stock within the same syngen. Successful intersyngenic transfers were observed for mu from stock 138 of syngen 8 to stock 540 syngen 1 (and vice versa), and kappa (51) of syngen 4 to syngen 2. However, mu symbionts did not grow in syngens 2 and 4, nor did kappa in syngens 1 and 8. In all cases control injections were carried out using homogenates or other cell fractions including mitochondrial and post ribosomal fractions from paramecia without endosymbionts. Post-ribosomal fractions from cells with endosymbionts were also unsuccessful in bringing about the establishment of endosymbionts. The possibility that a gene for maintenance is being transferred during microinjection has been ruled out by the following experiment.

Cytoplasm from paramecia without symbionts but which possess the gene was injected into some cells lacking the gene, for example stock 299 into stock 138. Microinjection of stock 299 lambda symbionts into the stock 138 survivors never resulted in the establishment of endosymbionts. Incidentally, successful microinjection of endosymbionts into paramecia which previously contained the same symbionts has been recorded (Table 3). Several experiments have been carried out where endosymbionts were transferred from one paramecium to another with different endosymbionts (Table 2).

The maintenance of a particular endosymbiont depends on environmental conditions and on the presence or absence of a nuclear gene. Successful injection implies the presence of a specific symbiont-supporting gene in the recipient. Cells which do not grow the symbionts following injection would then lack the gene. The exchange of kappa particles between syngens 2 and 4 and mu between 1 and 8 would mean that the gene in the recipient cell can function with close relatives of the resident endosymbionts or else that there is a second gene in the recipient similar to that of the donor cell. I therefore examined the effect of the nuclear gene on symbiont maintenance. Different symbionts were injected into stocks which have recently lost the maintenance gene as determined by breeding experiments and results are shown in Table 3.

It is clear that in some cases endosymbionts can be transferred to cells without the gene and that they persist through many (>100) fissions. These cells were tested by mating to paramecia with the endosymbionts and were shown to lack the gene, as judged by the appearance of 1:1 segregation of clones which maintain or lose endosymbionts in the F_2 generation. Evidence for the gene which does not allow maintenance of mu 540 in stock 513 has been recorded elsewhere[9], and the presence of a gene which does not allow alpha maintenance (here in stock 576) has also been recorded[2].

The presence of the gene which could not maintain kappa 51 was shown by making a cross between stock 51 (with kappa) and stock 116. Following autogamy of the hybrid, an F_2 was obtained comprising 25 clones capable of maintaining kappa and 30 unable to do so, indicating a 1:1 ratio as would be expected for segregation of a pair of alleles. In some experiments there was no gene difference between stocks 131 and 138 in terms of maintenance of mu 138[1]. By contrast, I have found a gene difference between the two stocks. Stock 131 also possesses a gene which does not allow lambda 299 to grow in the cytoplasm.

The most surprising result, however, is that with the exception of mu 138 and mu 540 which seem to be interchangeable, the resident symbionts only can be maintained in cells which lack the specific maintenance gene. For example, it is possible to transfer mu 540, lambda 299 or alpha 562 to paramecia which have recently lost the same endosymbiont following replacement of the particular maintenance gene during breeding. This result is similar to the long term maintenance of endosymbionts in the absence of the gene as described elsewhere[10].

However, successful injection of alpha, lambda, and mu only takes place in such cells if they are not "older" than twenty, thirty and twenty fissions respectively following gene replacement. Cells at later fissions following replacement of the gene do not accept the endosymbiont which was previously present. This result suggests either that the genes for maintenance are still active for a certain period, then become inactive or that genes which prevent the growth of symbionts become active after a delay. The maintenance gene in the latter case is inactive and the alternative allele produces an inhibitor which functions to prevent the survival of the endosymbionts. To explain the infection of stocks 131 and 116 which will possess this active gene and also the fact that successful injections can only occur over twenty fissions, we must also postulate that the gene is only active under certain conditions.

In summary, symbionts can be microinjected successfully between paramecia independently of the presence or absence of the major gene, stock and even syngen. Such results may seem to suggest that the growth and replication of the endosymbionts do not depend on specific genetic factors or, alternatively, that a similar gene is present in different syngens and protozoa.

Symbionts have been introduced into another protozoan, *Didinium*[10,11]. The symbionts can also grow *in vitro* in the absence of the genes with a similar growth rate as *in vivo*, showing that the locus does not control the growth rate[12]. Opposite conclusions were reached in infection experiments

Table 2 Injection of Symbionts into Paramecia with Other Symbionts Present

	Symbionts injected						
Recipient cells*	Mu (540)	Mu (138)	Lambda (299)	Kappa (51)	Alpha (562)	Kappa 7	Kappa A_1
Mu 540	– (10)†	√ (9)	√ (31)	√ (26)	√ (20)	√ (9)	√ (15)
Mu 138	√ (15)	– (7)	0 (15)	√ (18)	√ (6)	X (12)	√ (9)
Kappa 51	√ (8)	√ (15)	√ √ (6)	– (9)	√ √ (8)	√ (7)	√ √ (10)
Lambda 299	√ (21)	√ (18)	– (2)	√ (8)	√ (5)	X (15)	X (11)
Alpha 562	√ (10)	√ (21)	√ √ (15)	√ √ (15)	– (19)	√ √ (8)	√ (12)

– =Impossible to tell if maintained as same symbiont injected. However, injection carried out as a control and symbionts were maintained in all cases.
√ √ =Both symbionts retained.
√ =Resident symbiont only retained.
X=Injected symbiont only retained.
0=Neither particle retained.
* At least twenty cells were injected and the results represent all the survivors in each injection.
† Actual number of survivors which maintain or reject injected symbiont.

Table 3 Injection of Symbionts into Paramecia which Have Recently Lost Symbionts

	Symbionts injected						
Recipient cells*	Mu (540)	Mu (138)	Lambda (299)	Kappa (51)	Alpha (562)	Kappa 7	Kappa A_1
$\frac{540}{513}$	√ (25)†	√ (29)	0 (34)	0 (32)	0 (17)	0 (16)	0 (15)
$\frac{138}{131}$	√ (29)	√ (18)	0 (29)	0 (18)	0 (19)	0 (15)	0 (11)
$\frac{51}{116}$	0 (10)	0 (17)	0 (7)	√ (17)	0 (25)	0 (13)	0 (8)
$\frac{299}{131}$	0 (15)	0 (15)	√ (19)	0 (16)	0 (23)	0 (12)	0 (17)
$\frac{562}{576}$	0 (30)	0 (20)	0 (15)	0 (20)	√ (15)	0 (9)	0 (4)

* Cells which lost symbionts in the 20 asexual fissions before injection. These were produced by mating cells with endosymbionts to those without and passing F_1 clones through autogamy. Where one gene is involved in maintaining the symbionts this breeding programme results in clones of cells which lose their symbionts. At least 20 cells were injected.
† Number of cells injected which survive and which show maintenance or absence of symbionts.
√ =Symbiont injected in 100% of cases.
0=Symbiont rejected in 100% of cases.

and genetic experiments where a specific gene was deemed to be necessary for the growth and reproduction of the symbiont[1,7].

My results are consistent with the presence of a genetic locus which is involved with the maintenance of endosymbionts. It is not clear, however, if the activity of the locus involves, (1) protecting the symbiont from destruction during the early fissions after conjugation or infection, or (2) producing a destructive agent which prevents the maintenance of the symbionts. Also the results presented here make it necessary to postulate that the gene may not always be active. The apparent specificity of a locus for one endosymbiont is still consistent with either mechanism.

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Cyclophosphamide: Induction of Superovulation in Rats

THE number of ova released at ovulation in rats varies within a narrow limit, usually between 10 and 15. Factors which maintain this relative constancy are not known. Several agents capable of inhibiting ovulation are known[1,2], but apart from gonadotrophin injections there appears to be no way to increase the normal ovulation rate[7]. An agent capable of doing this might be useful in improving breeding potential of laboratory or farm animals, and provide a tool for the study of the neuroendocrine basis of superovulation. (Superovulation is defined as an increase in the ovulation rate beyond that found in the controls.) Exposure of mice[3], rats[4] and hamsters[5] to X-rays has been found to increase ovulation rate and/or litter size. As radiomimetic agents[6] duplicate several effects of X-rays, they might be expected to induce superovulation in rats. Only cyclophosphamide (CPA) amongst those we tested had this effect.

Adult sexually mature rats (Wistar strain) were maintained under controlled environmental conditions of light (from 0600 h to 2000 h) and temperature (22° C). Vaginal smears were taken daily and rats which had at least one and frequently more consecutive 4 day oestrous cycles were included in the study. One group of five rats received a single oral dose of CPA (50 mg kg^{-1}) in 0.2 ml. of 0.5% 'Tween 80' in saline, the other received vehicle alone. The progression of oestrous cycles following CPA treatment remained unaffected and all treated animals showed cornified smears as in controls on the expected day. When rats were killed on this day, about 100 h after CPA administration, the number of tubal ova recovered from the CPA treated rats was significantly higher than from the control rats (Table 1). The uterine and ovarian weights of the treated rats were comparable to those of controls (Table 1). Except for a slight loss in the body weight (4.2%) no other side effects of the treatment were observed. When this experiment was repeated, the mean ovulation rate in the treated rats was 17.2±1.3 ($n=5$) which was again significantly higher than that in the control rats (10.5±0.5; $n=23$). When the drug was administered on other days of the cycle, metoestrus, dioestrus or pro-oestrus, it failed to increase ovulation rate and the length of the treated cycle remained unaffected. Increasing the dose to 100 mg kg^{-1} also failed to cause any further increase in the number of ova shed. Histological examination of serial sections of ovaries of rats treated with CPA and killed on the morning of oestrus showed increased numbers of freshly formed corpora lutea as expected. No luteinized follicles with entrapped ova could be found.

Table 1 Effects of Oral Administration of CPA on Ovulation Rate in Rats

Group	n	Ovulation rate	Ovarian wt (mg)	Uterine wt (mg)
Control	5	12.2±0.37 (11–13)	73.3±5.7	519±33
CPA treated	5	17.6±1.29* (15–22)	81.7±3.0	457±34

* $P<0.01$ when compared with control.

CPA (50 mg kg^{-1}) administered on day of oestrus. All animals had tubal ova. Values, mean±s.e. Figures in parentheses denote range.

To determine whether ova shed in the CPA treated rats were physiologically normal and capable of fertilization and implantation, the experiment was repeated but females were housed with fertile males on the night of first pro-oestrus following CPA treatment. Mating was confirmed on the following morning by finding spermatozoa in the vaginal smear (day 1 of pregnancy). At autopsy on the ninth or fourteenth day of pregnancy, the numbers of implantation sites and corpora lutea were found to be significantly higher than in controls (Table 2). A gross examination of embryos revealed no abnormalities. Embryo loss, that is the disparity between the number of corpora lutea and implantation sites, was significant in the CPA treated rats ($P<0.05$) but not in the control animals, and it seemed to increase with advancing gestation. This may be due to crowding of embryos in the uterus with an increase in competition for nutrients. Increased embryo mortality is also known to occur in animals superovulated with gonadotrophin treatment[7].

Table 2 Effects of CPA on Number of Corpora Lutea and Implantation Sites in Rats

Parameter	Autopsy on day 9 Control	Autopsy on day 9 Treated	Autopsy on day 14 Control	Autopsy on day 14 Treated
No. of rats	9	9	15	10
No. corpora lutea	13.1±0.7	18.4±1.0*	12.2±0.4	18.6±1.4*
No. implantation sites	12.0±0.4†	16.7±1.0‡	11.4±0.4†	15.0±1.0‡

* $P<0.01$ when compared with the contemporary control group.

† Not significantly different ($P>0.05$) from the number of corpora lutea in the same group.

‡ Significantly different from the number of corpora lutea in the same group.

Oral administration of CPA, 50 mg kg^{-1}. Values, mean±s.e.

The data show that a single oral administration of CPA at an appropriate stage of the oestrous cycle markedly increases ovulation rate. This may result either from an increased gonadotrophin secretion from the pituitary, permitting maturation of increased number of follicles, and/or from decreased rate of atresia of ovarian follicles. We believe this is the first report of a chemical substance unrelated to gonadotrophins capable of increasing ovulation rate.

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Effect of Multiparity on Human Maternal Hypersensitivity to Foetal Antigen

Although the infant possesses histocompatibility antigens which differ significantly from those of the mother, the foetal allograft manages to survive the period of gestation without being rejected. To explain this apparent paradox of transplantation immunology, Medawar in 1953 advanced several hypotheses[1]. These included (1) that the uterus may be an immunologically privileged site; (2) that the foetal antigens are weakly expressed; (3) that there may be an anatomical barrier separating the maternal and foetal circulations, and (4) that pregnancy may be accompanied by some reduction in the immunological capacity of the mother. We have attempted to evaluate one aspect of this problem using an *in vitro* correlate of cellular hypersensitivity to study the immunological response of the mother's lymphocytes to those of her infant. This technique, the macrophage migration inhibition assay[2], measures the elaboration of a soluble material, migration inhibitory factor (MIF), from sensitized lymphocytes after stimulation by specific antigen[3,4]. Previous work with mice has shown that when peritoneal exudate cells from two genetically different strains were mixed together for 24 h their migration was not inhibited, that is, no MIF was generated, unless one strain had been previously sensitized to the other[5]. In these conditions, the assay appeared to be measuring a cellular immune response indicating prior sensitization. This is in contrast to the response observed in the standard mixed lymphocyte reaction which measures at 5 days the incorporation of ^{3}H-thymidine into lymphocyte DNA. The latter response records an event of primary sensitization between lymphocytes of individuals with different histocompatibility antigens.

Table 1 lists the clinical data from the mothers and infants studied. Normal unrelated individuals with no history of transfusions served as controls. In addition, two patients with histories of multiple transfusions and one patient who had received a kidney graft were also studied.

The method for the production of MIF by human peripheral lymphocytes has been described previously[6]. Briefly, heparinized blood was sedimented, and the lymphocytes were separated from the monocytes and polymorphonuclear leucocytes by means of cotton columns. The lymphocytes were washed and the cell count adjusted to 3×10^6 lymphocytes/ml. Cells from each donor were cultured separately in medium TC-199 (free of serum or antibiotics) as well as being mixed with cells from other individuals in a 5:1 ratio (responder : stimulator). Cell-free supernatants were harvested daily for 3 days, concentrated and assayed for MIF activity on normal guinea-pig macrophages in capillary tubes[6]. The migrations were drawn at 24 h, the area was determined by planimetry, and the percentage migration was calculated using the following formula

$$\%\ \text{migration} = \left\{ \frac{\text{area of migration } \overline{xy}}{(\text{area of migration } \bar{x} + \text{area of migration } \bar{y})} \right\} /2$$

where x is in supernatants from cultures of responder cells; y is in supernatants from cultures of stimulator cells; xy is in supernatants from cultures of *mixtures* of responder and stimulator cells. Supernatants were assayed on cells from two or three guinea-pigs, and the areas of migration from four or six capillaries were averaged.

Results of the MIF assay in cultures obtained from normal and experimental subjects are illustrated in Table 2. It can be seen that lymphocytes from control subjects with no previous history of transfusions, when mixed with lymphocytes from unrelated individuals, did not produce substances during culture that were inhibitory to guinea-pig macrophages. The mean percentage migration for the group was 101.9±9.9 (s.d.). Migration less than 81%, 2 s.d. below this mean, was considered positive and indicative of MIF production. To determine whether we could detect prior sensitization, three patients, two with histories of multiple transfusions, and one, a recipient of a kidney graft, served as potential positive controls (the latter was tested with lymphocytes from the kidney donor).

Maternal lymphocytes from five out of ten patients (M. Q., D. F., V. C., M. S., M. M.) produced MIF when incubated in the presence of their infants' lymphocytes. In addition, two of these mothers were tested against lymphocytes from unrelated donors and did not produce MIF. The only distinction between mothers whose lymphocytes made MIF and those who did not was their parity (see Table 1). All five of the

Table 1 Clinical Data

Patient	Age	Parity	Transfusion history	Maternal blood type	Gestational age (weeks)	Sex	Infant birth weight (g)	Abnormality
D. R.	18	I	0	A+	41	M	3,550	Normal
R. T.	23	I	0	O+	38	M	3,020	Normal
G. G.	19	I	0	AB+	39	F	3,500	Normal
K. M.	22	II	0	A−	38	M	3,250	Coombs-Rh+
D'Ag	22	III	Multiple* 1963	B+	39	F	3,400	Normal
D. F.	29	III	0	A+	40	F	3,501	Ventricular septal defect
V. C.	21	III	0	O+	40	M	4,100	Normal
M. M.	33	III	1–1968	B+	39	M	3,300	Normal
M. S.	23	V	1-post partum	A+	38	M	4,000	Normal
M. Q.	22	VII	0	A+	18	M	400	Normal

* Received radiation therapy for carcinoma of ovary.

Table 2 Percentage Migration

	Normal subjects *	Patients †	Mother-baby ‡	Baby-mother ‡
	98	79	87	97
	98	76	90	117
	96	75	101	111
	93		87	91
	122		97	106
	112		68	110
	100		71	96
	101		71	109
	98		76	102
	91		62	89
Mean ± s.e.m.	100.9 ± 2.8	76.7 ± 1.2	81.0 ± 4.0§	102.8 ± 2.8

MIF production in control subjects and patients. Supernatants obtained from mixed lymphocyte cultures in the absence of serum (responder: stimulator ratio being 5:1) were assayed for MIF activity. Migration below 82% is significant. All mothers whose lymphocytes produced MIF in response to their babies' lymphocytes had three or more pregnancies.

* No previous blood transfusions.

† Two patients with multiple blood transfusions and one kidney recipient.

‡ The MIF results for each mother and infant are listed in the same order that is given in Table 1.

§ Mean percentage migration with three or more pregnancies is 74.2%±4.9; mean percentage migration with less than three pregnancies is 91.3%±3.3 (difference of mean migrations statistically significant by the Student t test for paired means = $P<0.05$).

mothers whose lymphocytes were sensitized to those of their infants had been pregnant three or more times. In all but one where sensitization was not detected, the mothers were in their first or second pregnancy. The one exception was a gravida three para three woman who had received X-irradiation and chemotherapy for an embryonal cell carcinoma of the ovary seven years prior to the current pregnancy. These therapeutic modalities may have altered the patient's cellular immune response. It was also interesting that when infants' lymphocytes were mixed in a 5:1 ratio with maternal lymphocytes, no MIF was made, that is, there was no evidence of sensitization of the infants' to the mothers' cells.

These data demonstrate that cellular hypersensitivity to the infant is present in some mothers during pregnancy. Therefore, the success of the foetus as an allograft is not a result of immunological paralysis as previously suggested[7]. But the question remains: what is the mechanism which allows foetal survival in these conditions? Recent studies have suggested that the maternal "tolerance" during pregnancy may be mediated through serum factors. The Hellströms, for example, have shown in mice that maternal serum contains an enhancing factor which abrogates the cytotoxic effect of maternal to foetal cells[8]. Further, Ceppellini has demonstrated a factor in maternal serum which suppresses the autologous and homologous responses in the mixed lymphocyte reaction[9]. Our studies were carried out in the absence of serum and, therefore, such factors would not mask the production of MIF. It remains to be determined whether preincubation of foetal cells with maternal serum would block the subsequent production of MIF by sensitized maternal lymphocytes.

In the studies reported here, MIF production seemed to reflect prior sensitization. Others, however, have detected an inhibitory activity in supernatants obtained from mixtures of nonsensitized cells[10,11]. Bartfeld and Atoynatan[10] required 2.5–5 times more cells than in the present study to elicit "MIF production" in mixtures of nonsensitized cells; in the experiments of Phillips *et al.*[11] a longer time course was also required. It is possible, therefore, that these workers may be detecting primary allograft sensitization reactions which our technique is not measuring either because of differing experimental conditions or because it is less sensitive.

In conclusion, in the experimental conditions used in this study, it has been possible to demonstrate that cellular hypersensitivity to the infant is present in some mothers during pregnancy and, further, that the incidence of maternal lymphocyte sensitization increases with the number of pregnancies. The sensitization of the mother by foetal erythrocytes resulting in rhesus sensitization is a well known phenomenon. Exposure of the mother to foetal cellular antigens during gestation with antigens passing from the foetal to the maternal circulation may be the source of the maternal sensitization herein observed. Such crossing of the placenta by maternal and foetal antigens has been described[12,13].

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Bladder Cystitis following Focal Infection of Group A Streptococci

Foci of infections have long been recognized as the cause of certain systemic diseases. In 1915, Rosenow studied the localization of streptococci after i.v. injection[1]. Subsequent studies have shown that viable streptococci and/or their metabolic products localize in nearly every organ and tissue[2-6].

The localization of Group A streptococci in relation to the urinary bladder is of general interest. Meisser and Bumpus[7] found bladder lesions after i.v. injection of a "streptococcus". Much interest in the field of urology has been generated over the aetiology of interstitial cystitis or Hunner's ulcer, which is almost exclusively a disease of women. Evidence from our laboratory has shed some new light on the possibility of the causative factor being a Group A streptococcus[8]. Using immunofluorescent techniques streptococcal antigens were demonstrated within the bladder wall following subcutaneous injections of lyophilized *Streptococcus pyogenes* Group A, Type 12, in the back of rabbits. Microscopic examination of these bladders showed chronic lesions characterized by inflammatory cell invasion, general tissue injury and alteration, fibrosis, bladder contraction, depletion of DNA fluorescence, and circulating anti-DNA antibodies, which showed many similarities to human interstitial cystitis. No viable streptococci were present. Preliminary studies have shown a sex difference in these lesions with female rabbits evidencing a severe bladder lesion in contrast to males.

We report this in view of the severity of Group A streptococcal involvements in other diseases such as rheumatic fever, glomerulonephritis and their complications.

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Tryptophan Excited States and Cataracts in the Human Lens

We present here a study of the fluorescence and phosphorescence of human eye lenses *in vitro* with regard to the mechanisms of formation of cataracts. Light transmission by the cornea decreases rapidly with decreasing wavelength, and is essentially zero for wavelengths less than 293 nm[1-3]. The important effect of this corneal absorption was demonstrated by Bachem[3] who induced cataracts in guinea-pigs and rabbits with ultraviolet light and presented an action spectrum to show that the efficiency of *in vivo* cataract production rose steeply, from zero at 293 nm to maximum at 300 nm, and then fell off sharply at 313 nm with a long tail extending to about 365 nm. This action spectrum and the corneal absorption spectrum are shown in Fig. 1.

We used normal lenses obtained from the Eye Bank, and cataractous lenses obtained directly from surgery. Lens specimens from donors aged 39–81 years were placed in sterile Ringer's solution, immediately in the case of cataracts from surgery, and within 45 min of death in the case of normal lenses. The solutions were then frozen to dry ice temperature, and kept until needed. Measurements were made from within a day to within a month of enucleation. For spectroscopic emission studies, the samples were mounted in quartz cells. The excitation beam from a new 1,000 W xenon arc lamp passed through a Bausch and Lomb compact grating monochrometer, producing an excitation band width of about 7.5 nm. The emission was observed at right angles through a second 'Bausch and Lomb' monochrometer, and detected photoelectrically with a '1P28' phototube, the output of which was recorded on an X-Y recorder. A rotating can phosphoriscope was used to separate short lived fluorescence emission from long lived phosphorescence emission. (The spectra presented have not been corrected for lamp output or phototube wavelength dependences. When these corrections are made, the phosphorescence excitation maximum is shifted about 5 nm to the blue and the phosphorescence emission peaks are each shifted about 5 nm to the red.) Absorption spectra were measured on a 'Cary 14' spectrophotometer. Intact lenses were pressed between quartz plates to adjust the optical density for these measurements.

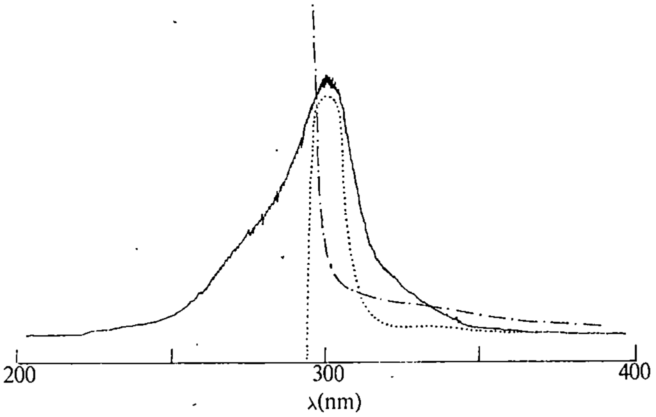

Fig. 1 Phosphorescence excitation spectrum of a healthy intact human lens at 77 K. The emission is monitored at 440 nm. ——, Excitation spectrum; . . . ., action spectrum of Bachem[3]; — · — · —, corneal absorption.

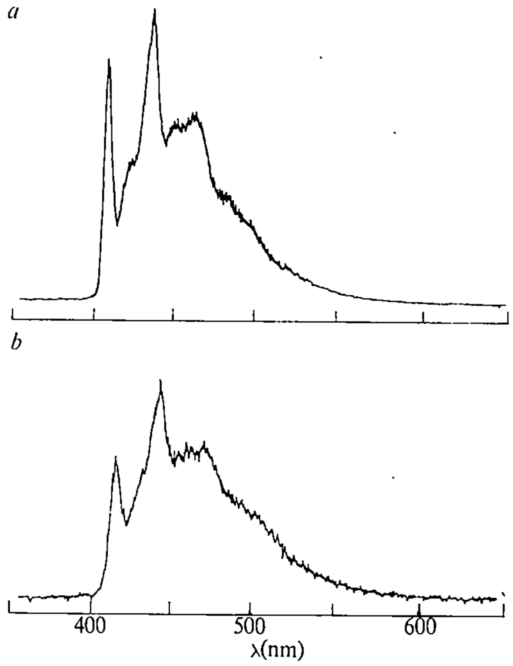

Fig. 2 *a*, Phosphorescence emission of tryptophan in ethanol-water solution (10^{-3} M) at 77 K, excited at 300 nm. *b*, Phosphorescence emission of an intact healthy lens at 77 K, excited at 300 nm.

We have measured the phosphorescence spectra of intact human lenses at 77 K, and find a characteristic emission spectrum (Fig. 2). This spectrum is independent of exciting wavelength in the range 250–313 nm. (For excitation wavelengths longer than about 313 nm, the phosphorescence emission changes from that shown in Fig. 2 to a broad structureless spectrum with a maximum at about 520 nm.) This phosphorescence was compared with that of tryptophan and we concluded that the former originates from tryptophan residues in the interior of a protein, and not from the free amino-acid (Fig. 2). This is shown by the redshift of the peaks in the lens phosphorescence spectrum[4] and by lens fluorescence data (ref. 5 and Staton and Borkman, unpublished data).

At 77 K, the phosphorescence of tryptophan in EPA or ethanol-water glass was found to have a lifetime of 7.0±0.5 s, while that of the normal lenses was 4.6±0.5 s, and that from a brunescent cataractous lens was found to be 5.2±0.5 s. Decay data on large numbers of normal and cataractous lenses are needed to improve the precision of the lifetime measurements. Our data, however, clearly show that the lens emission originates from tryptophan within a protein, and not from the free amino-acid[5]. They also suggest the possible use of emission lifetimes as a new criterion for characterizing cataracts. The change in lifetime between a normal and a cataractous lens could result either from the presence of a new phosphorescence species, or from the fact that the local environment of tryptophan[5] may be different in normal and cataractous lenses.

Monitoring the tryptophan-like lens phosphorescence at 440 nm, we obtain an excitation spectrum peaking at 300 nm as shown in Fig. 1. After correcting for the wavelength dependence of our excitation lamp output, we find the maximum in the phosphorescence excitation spectrum to be at 295 ± 5 nm, a range which clearly overlaps the wavelength reported by Bachem[3] for maximum efficiency in ultraviolet cataract production. A good approximation to Bachem's action spectrum for cataracts can in fact be obtained by computing the product of the corneal transmission spectrum and our lens phosphorescence excitation spectrum. This demonstrates the potential importance of the excited states of tryptophan as intermediates in lens photodamage. This idea is supported by the fact that tryptophan is known to be very photo-reactive, both in the free state and in proteins; it forms coloured products under ultraviolet irradiation, even at liquid nitrogen temperatures[6].

An effort was made to identify the tryptophan excited state(s) potentially significant in lens photodamage. We reasoned that a fast photochemical process originating from the excited singlet state of tryptophan would result in fluorescence quenching, but that a fast photochemical process originating from the triplet state would result in quenching of phosphorescence. At 77 K our emission spectra show that the lens fluorescence and phosphorescence quantum yields are both large (about 20%) and about equal to each other. We conclude that neither excited state emission is strongly quenched under these conditions. However, at room temperature we observe no phosphorescence from human lenses (at least 100 times weaker than at 77 K), and therefore, under these conditions, the triplet state energy tryptophan must be dissipated by processes other than light emission; chemical reaction, energy transfer, or radiationless transitions. These considerations suggest that at room temperature tryptophan excited triplet state is the intermediate in lens photodamage. On the other hand, we (and others[7]) have observed that the fluorescence of tryptophan in ethanol-water solvent at 25° C is quenched (by a factor of 2) in an aerobic solution compared to a vacuum outgassed sample. Barenboim has claimed that the mechanism of this quenching is enhanced intersystem crossing from the excited singlet to the triplet state of tryptophan[7] and proteins containing tryptophan can take up oxygen under ultraviolet irradiation[8]. We find that irradiation of a tryptophan solution in ethanol water solution at 25° C under aerobic conditions for 16 h with 313 nm Hg line produces visibly coloured products. The absorption spectra of these products were found to be in agreement with those of the adult human lenses we studied. That these new species were photo-oxidation products was shown by irradiation of a degassed tryptophan sample for 16 h without the formation of products, as determined by ultraviolet absorption and thin layer chromatography (TLC). These fluorescence-quenching and photochemical results suggest that the excited singlet state of tryptophan may also be important in lens photodamage and that the degradative reaction is a photo-oxidation.

Our TLC measurements showed that air photo-oxidation of tryptophan results in two products. Gomyo and Fujimaki[9] have recently demonstrated the sensitized UV-photo-oxidation of tryptophan in lysozyme, and have identified two photoproducts as kynurenine and 3-oxykynurenine. Van Heyningen[10] has isolated three fluorescent compounds from the normal human lens and has identified two of them as free kynurenine and a glucoside of 3-hydroxykynurenine. We and others[11] have observed that the absorption and fluorescence intensities are greater in brunescent cataracts than in normal lenses. It seems likely that this lens pathology is attributable to an excess of tryptophan oxidation products, generated enzymatically, or, as we have shown, photochemically.

Gomyo *et al.*[9] showed that tryptophan photo-oxidation in lysozyme caused a change in protein conformation resulting in decreased water solubility. A similar decrease in the solubility of lens protein following tryptophan photo-oxidation could induce opacity in the lens. The low solubility of brunescent lens proteins, relative to proteins in other types of cataracts, has been noted[11], and the increase in the insoluble protein fraction with onset of cataracts in general is well known[12].

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Indices of Discriminability

Hammerton and Altham[1] have pointed out the desirability of having a numerical measure for the discriminability of two stimuli, A and B, that does not depend upon the specific assumptions about the probability distributions of the internal events produced by A and B. Assuming that the data consist of confidence ratings for A and B, they have proposed an index *C*, which is equal to the difference between the average ratings for A and B divided by the difference in the ratings that represent "certainly A" and "certainly B". Unfortunately their definition assumes that at least one rating can represent "certainly A" and at least one rating can represent "certainly B". This often does not happen. For example[2], when observers were permitted to develop their own rating systems for visual stimuli, it was found that for stimuli consisting of 55 and 66 quanta, on the average, at the cornea, there was not a single rating that meant certainly one stimulus or certainly the other. Another way of saying this is that there was never a single trial on which the observer was certain that the stimulus was the strong one.

Their index could still be applied if one divided instead by the difference between the smallest rating used for stimulus A and the largest rating used for stimulus B. However, it is incorrect to suggest that the smallest rating used for the weaker stimulus A means "certainly A" because it may sometimes be given in response to B. Their index is actually the difference in the mean ratings for A and B divided by the range of ratings used (minus one). This is somewhat unsatisfactory because if the mean rating and range of ratings are fixed, then *C* is completely determined. But if only the variances of the distributions decrease, then discriminability will increase although their index *C* will remain unchanged.

The desirable properties that a discriminability index should include are (1) a simple interpretation that is independent of any assumptions about the underlying distributions; (2) independence from the particular units used for the ratings; (3) ability to compare different observers doing the same task and the same observer doing different tasks; (4) the index should be a function of the parameters that are necessary to specify discriminability. It must change when discriminability changes.

The index *C* does not have the fourth property because it is independent of the variances of the distributions. The index d' fails the fourth condition because it only depends on the variance of one of the distributions. Also, as pointed out by Hammerton and Altham, there is a weak implication that the underlying distributions of internal events are Gaussian, although the measure could be used when this is not the case. In principle, one could avoid this difficulty by redefining d' in terms of the horizontal intercept of the ROC curve on double probability paper or by using the index d'_e which is measured along the diagonal. But for non-Gaussian distributions, the interpretation of these indices may be extremely unclear so condition (1) is not really satisfied.

I propose, therefore, a new index *D*, the Standard Separation

$$D_{(A,B)} = \frac{\bar{i}_{(B)} - \bar{i}_{(A)}}{\sqrt{S_{(A)}\,S_{(B)}}}$$

where $\bar{i}_A$ and $\bar{i}_B$ are the average ratings for A and B, and $S_{(A)}$ and $S_{(B)}$ are the standard deviations of the respective rating distributions. Random ratings would produce $D = 0$ and perfect discrimination would produce an infinite *D* providing that the observer used only one rating (zero variance) for at least one of the stimuli. The index *D* satisfies conditions (1), (2) and (3) and also satisfies (4) better than the indices *C* or d', since it depends on the variances of both distributions. Of course, in principle, discriminability may depend on even higher moments, but in practice *D* may be completely sufficient.

There is also another older index that satisfies all four conditions. That is P_C, the percentage correct in a two alternative forced choice experiment, which is perhaps closest to what is meant by discriminability. In order to measure what P_C would have been from confidence rating data, one either measures the area under the ROC curve[3] or simulates the experiment[2]. This is independent of the Gaussian assumption.

The suggested new index *D* is applicable in a great variety of circumstances and may be the most generally applicable measure but P_C is also a generally valid measure. Under circumstances where the distributions are approximately Gaussian, and of equal variance, *D* is equal to d'.

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Transition Probability and Dichotic Listening

BLOOMFIELD[1] has rejected the hypothesis that in a dichotic listening situation the selection of the attended message by the subject is based only on spatial cues, and argued that the transition probabilities between words also affects their selection. Physical cues rather than spatial ones should have been referred to because it has been demonstrated that selection can be made in the absence of spatial cues if the two messages are presented in distinctly different voices[2]. Only the variety of the rejected hypothesis which also postulates simultaneous analysis of the unattended message is considered in the theoretical treatment of results. If attenuation of the secondary channel and selection on the basis of physical cues only are postulated[3], then words presented in the secondary channel have a reletively high recognition threshold. Without contextual information potentially gained from previous words, the instruction "tap" does not have a lowered threshold and we would not expect it to be heard. Our hypothesis contradicts Bloomfield's conclusion, although it is compatible with his data. Also in the presence of unequivocal physical separation (messages presented to different ears in different voices[3]) listeners never reported items from the secondary message. A strong stimulus set overrides even a strong response set[4]. Changing the contextual probability within a message is not "known to result in switching to the alternative channel", as Bloomfield asserts; Treisman[3] has reported that "subjects occasionally repeated one or two words" from the secondary message when those words were more appropriate than those presented simultaneously in the primary message. Recognition of a word presented in the secondary message is only likely when that word is appropriate to the selected message. Presentation of an improbable word in the selected message may lower the recognition thresholds for more probable words presented in other messages, but this does not necessarily affect the threshold for other contextually improbable instructions such as "tap". Giving the listener a response set towards this word might reduce this threshold.

Words presented in the secondary message were more likely to be selected and repeated when they had a high transition probability with the preceding word in the primary message, and were responded to in preference to less probable words in the primary message. This may be a demonstration of the word-frequency effect in recognition thresholds[5,6]. Such words may gain a response as a result of "sophisticated guessing"[7,8] or a response bias[9]. When unattended words are probable in the context of the attended message, two sources of information are available to the listener. Preceding items restrict the set of probable alternatives and may lower the recognition threshold for this set, and stimulus information is available at the time of presentation. Although this information may be non-redundant or attenuated, in conjunction with the contextual information it may still be sufficient to enable a verbal response.

Bloomfield's hypothesis states that if selection is based upon both physical and contextual cues, then the relatively low probability of the instruction, in the secondary message, to tap will not "compete" with low probability words in the selected message. Selection will be based on physical cues alone. Although this argument differs from that above, the prediction is the same. When we consider only those occasions when correct shadowing (and, theoretically, attention to the primary message) was reported, then the tapping instruction was followed only when a highly probable word was presented simultaneously in the primary message. This is not in accord with Bloomfield's hypothesis, for a contextually probable word in the primary message should lead to selection of that message, and consequently the tapping instruction should not be heard. This can be explained in the theory of shared processing capacity[10]. This theory would argue that words which are highly probable require less processing capacity for their identification than do words which are improbable because the latter contain more information. The amount of capacity residual from analysis would therefore be greater in the case of highly probable words, and the difference in the amounts of processing capacity available for secondary tasks might have resulted in more efficient analysis of the word "tap" when the residual capacity was greater.

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Reply

IN my original article[1], I was concerned to juxtapose two different theories of dichotic listening. One of these is that the ears constitute two channels, only one of which can be fully analysed if items arrive at both simultaneously. The other theory, which I claimed was supported by my results, was that multiple criteria are used in the selection of items for analysis from a common, rapidly decaying auditory store. One criterion, of course, could be the ear at which the item arrived.

Underwood claims that Treisman's attenuation theory[2] could explain my results. The main finding I reported was that under left (shadowed) channel conditions where the subjects were likely to report a contextually more probable right channel item, they failed to obey a tap instruction in a second experiment. Appropriate tapping sometimes occurred, however, when the instruction coincided with a probable left-channel item that was successfully shadowed. I agree with Underwood that the last result calls for some notion of shared processing capacity[3], and I would have developed that point had space permitted. I do not agree, however, that Treisman's theory is capable of explaining why subjects did not respond to "tap" when it coincided with an unexpected item to be shadowed, although they often did tap appropriately while shadowing a high-probability word. A theory which supposes that the unshadowed channel is attenuated must predict a higher probability of tapping during the presentation of the low-probability item for shadowing.

My own view, already expressed, is that items are selected on both spatial and contextual cues, so that if context does not favour one of two coincident items selection for processing will proceed on spatial cues alone, causing the tap instruction to be ignored.

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Feature Detectors and Vernier Acuity

HUMAN subjects can achieve an accuracy in a vernier alignment task of a few seconds of arc visual angle in optimal conditions[1-3]. The inter-cone spacing in the central fovea is several times this magnitude[4], so this performance must be achieved through some spatial information processing in the visual system.

Theories of vernier performance have concentrated on the problem of locating the position of the retinal image of one of the lines (that is, specifying the x coordinate in Fig. 1) to the requisite accuracy. Two explanations have been suggested. The first[2,5] depends on the intensity differences at a receptor created when the retinal image of a line (modified by the optics of the eye[6]) is given a small displacement (the illumination gradient hypothesis). The second theory[7] assumes each receptor, instead of giving a graded signal, only signals whether or not it is illuminated. The requisite accuracy is achieved by averaging over the length of the line to establish a "mean retinal local sign".

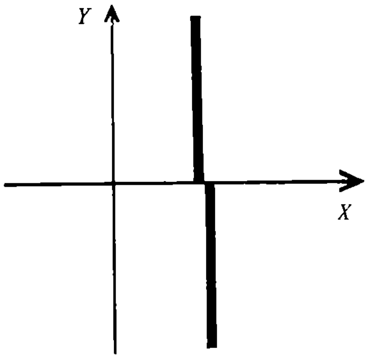

Fig. 1 The vernier acuity task. The subject makes an alignment setting by moving one of the lines along the x axis.

Neither theory is more than indirectly supported by the experimental evidence. The improvement of vernier acuity with target luminance provides some support for the illumination gradient hypothesis[2]; but the maintenance of acuity when the target is blurred[8] is difficult to understand on this basis. The mean local sign hypothesis is supported by studies which find an effect of line length on acuity (ref. 7 and unpublished work of J. A. Foley-Fisher); but the sharp deterioration which is found if a separation is made between the vernier lines[9] is not easily explained by either theory.

An alternative hypothesis is suggested by recent work on the visual system. It has been established physiologically that pattern information is transmitted by neurones in the visual cortex, often termed "feature detectors", which respond specifically to the size and orientation of elements of the stimulus array[10,11]. The existence of similar units in the human visual system is indicated by work which demonstrates that humans possess "channels" selectively activated by stimuli of a particular size and orientation[12-14]. The amount of activation in a channel is determined by the contrast in the stimulus rather than the light intensity. Much current work is concerned with the elucidation of the properties of these channels and relating them to the more traditional areas of perception. Here I suggest an application of this approach to vernier acuity.

In the vernier task subjects on occasion report that they achieve their final alignment by the elimination of a "kink" at the junction of the lines. It seems possible that this might correspond to reduction of activity in a channel, as defined above, the axis of which is at an orientation oblique to the vernier lines. This is clarified in Fig. 2 which shows that the hypothesis is essentially one of contrast discrimination in such a channel. Contrast sensitivity increases as the spatial frequency

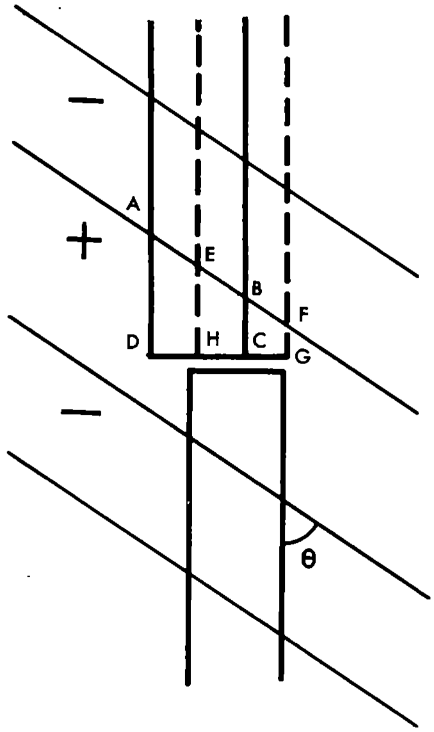

Fig. 2 The suggested hypothesis relating misalignment to activity in a cell the receptive field of which is oriented as shown at an angle θ to the vernier lines. There will be a change in excitation in the centre of the receptive field between the offset and the aligned positions, whereas the excitation of the surround will be unaffected. With the offset shown the change in excitation is equivalent to that produced by an area of target equal to the difference between the areas ABCD and EFGH. If the offset distance (DH) is d and the bar width (DC) is D, then this area is $d\ D$ cot θ. This result will not be greatly altered by the transformation produced by the optics of the eye. If the receptive field width is W, the misalignment excitation change will be a function d/W cos θ of the total produced by the stimulus. This can be regarded as equivalent to a Weber faction for the cell and, using plausible values for the variables, fractions between 1/200 and 1/30 are obtained.

of the channel decreases (down to 8 cycles per degree)[15], so it is not immediately clear whether high or medium spatial frequencies would be most effective.

The hypothesis implies that if the sensitivity of the oblique channel could be decreased, poorer acuity should result. A way of testing the hypothesis is then suggested by the method for desensitization of visual channels described by Campbell and Kulikowski[12]. They show that a high contrast grating target masks gratings of a similar orientation but has negligible effect on the detection of gratings of widely different orientations. This may be interpreted to mean that presentation of a high contrast grating effectively raises the threshold in a particular channel. Thus, in order to test the hypothesis, the effect of a high contrast grating background on a vernier acuity task was determined as the angle between target and background was varied.

The vernier target was generated on an oscilloscope screen by a computer and interface ('IBM 1130, WDV'). This was viewed at a distance of 2 m in a dark room. On a second oscilloscope with identical phosphor a sinusoidal grating was generated using the technique of Campbell and Green[15]. A large Dove prism was placed in front of this oscilloscope and the targets were combined optically. The subject was able to adjust one line of the vernier target in either direction by means of a series of buttons interfaced to the computer which also recorded the final setting. It was found in preliminary experiments that the largest effects were obtained with medium spatial frequency backgrounds and with the vernier target of low brightness. In the main experiment the background was a 12 cycle per degree grating, with average luminance 8 cd m^{-2} and contrast about 0.6 (defined as in ref. 11). The vernier target was always vertical and was set so that when the background was also vertical, the vernier lines were just detectable.

Six members of the department, naive as to the purpose of the experiment, served as subjects; all had normal or corrected vision. The subjects made settings in ten different conditions in which the background grating was at the following angles to the vernier lines: 90°: ±45°, ±30°, ±20°, ±10°, 0°. Ten settings were made in all under each condition in two blocks of five. The sequence of the resulting twenty blocks was randomized and different for each subject. Ten minutes of practice trials preceded the experimental trials which lasted about 50 min.

The measure of acuity taken was the standard deviation of the settings about the mean. The difference between the mean and the true alignment position was also recorded, but the systematic component of misalignment was found to be generally small with no consistent trends. The data on setting variability are presented in Fig. 3 for individual subjects, and Fig. 4 shows the arithmetic means of the six subjects in each condition. Analysis of variance shows the difference between conditions is significant at the 1% level and it is also evident from the symmetry of the data that this represents a genuine angular effect. The results are in accord with the prediction that a grating background oblique to the vernier lines would impair acuity. The maximum effect occurs with a grating oriented at 20° to the vernier lines. The tuning of human orientation sensitive channels[12] is 12°–15°, and so this result is consistent with the view that maximum alignment acuity is

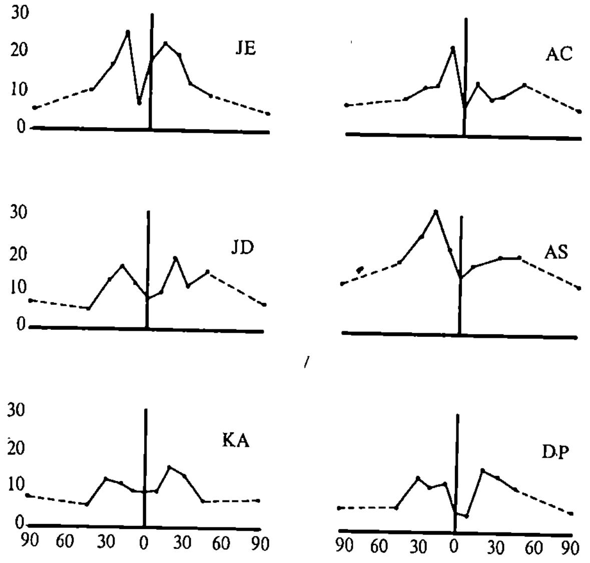

Fig. 3 Vernier acuity as a function of the orientation of a grating background. Individual results for six subjects. Each point represents the standard deviation of ten settings, measured in seconds of arc visual angle.

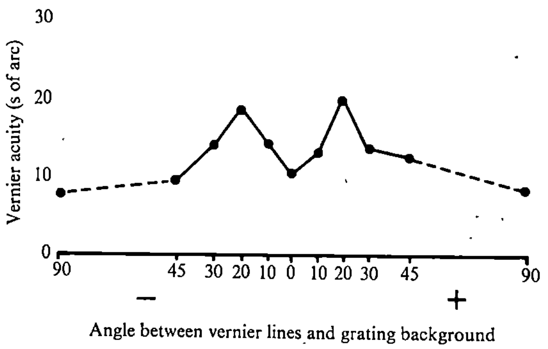

Fig. 4 Vernier acuity as a function of the orientation of a grating background. Means of the results shown in Fig. 3.

achieved by the detection of a change in the activation of an independent oblique channel.

But it is perhaps appropriate to conclude with two notes of caution. There is considerable similarity between the configuration of target and background which produces maximum acuity degradation and that which produced maximum shift in the Zollner illusion[16]. Thus the vernier lines in this situation are subject to a systematic illusion of tilt. It is nevertheless difficult to see why this should lead to any increase in the variance of the vernier settings, and indeed it is possible to provide an explanation of the Zollner effect in terms of feature detectors[17]. Finally, mention should be made of the finding of Ludvigh[18] that vernier precision can be maintained in a modified form of the vernier task which consists of aligning the middle one of three dots. This result presents a considerable problem for any theory of acuity.

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Effects of Marijuana and Tobacco Smoke on Human Lung Physiology

MOUSE lung explants exposed to smoke from cigarettes to which marijuana was added have been reported to display more cellular abnormalities than those exposed to smoke from cigarettes without marijuana[1]. We report here a study designed to test the effects of smoke from cigarettes made of marijuana only on human lung explants, and to compare these effects with those obtained after exposure to smoke from Kentucky Standard cigarettes.

We used the model system developed for preparing and exposing lung explants to puffs of fresh smoke in standardized conditions[2]. Fresh human adult lung tissue was obtained from men (45–56 yr) who had undergone surgery because of pulmonary tumours. For the lung explants pieces of "normal lung" were taken far distant from the tumour. Absence of tumour was established by microscope examination. The cultures, which at three to four weeks showed a regular monolayer of fibroblastic cells, were exposed in a 'Filtrona CSM 12' smoking machine to puffs of fresh smoke from marijuana cigarettes, or to puffs of whole fresh smoke, or smoke of the gas-vapour phase[2] from Kentucky Standard cigarettes. Marijuana cigarettes containing 1.8 g of marijuana (UNC 303, 0.6% tetrahydrocannabinol (THC)) for each cigarette were prepared with the same paper as that for Kentucky Standard tobacco.

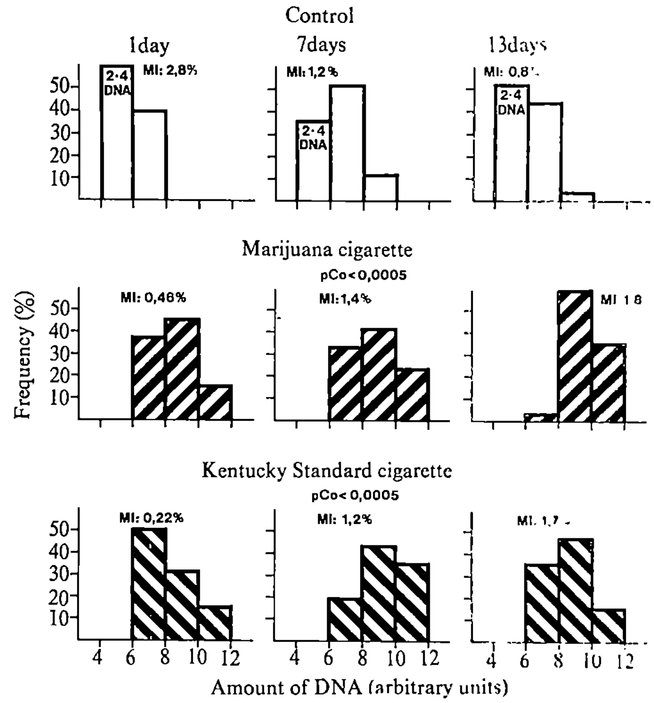
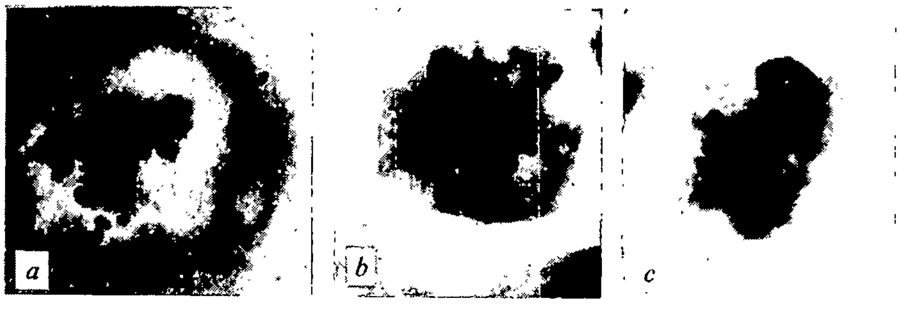


Fig. 1 Comparison between effects of fresh smoke from marijuana and Kentucky Standard cigarettes on the DNA content of fibroblastic cells in human adult lung explants, one, seven and thirteen days after exposure (Feulgen microspectrography). 375 cells measured. MI: Mitotic index.

Experiments were carried out on over 1,300 cultures of human lung explants. For each experiment a minimum of eight sets consisting of twenty-four coverslips with matched lung explants was used. Each set comprised a control culture not exposed to cigarette smoke, a culture exposed to four puffs per day (25 ml. at intervals of 58 s) of fresh smoke from marijuana cigarettes for 4–10 consecutive days, and a culture exposed in the same manner to two puffs from Kentucky Standard cigarettes. The lower number of puffs from Kentucky Standard cigarettes was given because of the relatively high cytotoxic effect of this type of cigarette on the cultures. The larger puff volume of 25 ml., instead of 8 ml. used in the previous study[1], was chosen because it resembled more closely the standard puff volume of 35 ml. inhaled by human smokers. Media were changed immediately after each exposure.

Fig. 2 *a*, Metaphase of fibroblastic cell in human adult lung explant, 6 days after 4 exposures to 4 puffs of marijuana cigarette smoke (H and E, ×1,000). Note tripolar metaphase with pieces of chromosomes lying distant from metaphase and the very large spindle. *b*, Metaphase of fibroblastic cell in human adult lung explant, 6 days after 4 exposures to 2 puffs of Kentucky Standard cigarette smoke (H and E, ×1,000). Note chromosome distant from main metaphase. *c*, Same culture as *b*. Anaphase, note lagging of chromosomes.



Chromosomal behaviour during mitosis was studied in live cultures under phase contrast and in the original stained cultures from 1–45 days after exposure. The mitotic index was obtained by counting all mitotic figures and relating them to the total number of cells of each monolayer grown on the coverslips. Frequency of mitotic abnormalities was obtained by counting all abnormal mitoses and relating them to the total number of mitosis in each culture. DNA metabolism was examined by autoradiography and Feulgen microspectrography[2–4].

Results were reproducible in all cultures. There were significant differences between control cultures and those exposed to smoke from marijuana and Kentucky Standard cigarettes (Table 1). From 1–4 days after exposure, cytotoxic effects such as pycnosis, necrosis and cell death were observed in the exposed cultures, accompanied by a striking decrease of mitosis and DNA synthesis. These early alterations were more marked after exposure to either whole smoke or the gas vapour phase of Kentucky Standard than they were after smoke from marijuana cigarettes. The lesser cytotoxic effect of marijuana, which contains a sticky resin, may perhaps be because cigarettes made from marijuana have a larger sidestream than Kentucky Standard cigarettes so that, in spite of the higher dose, less smoke *per se* reached the cultures[1]. Other alterations observed in surviving cells were essentially the same after exposure to marijuana and Kentucky Standard cigarettes. There was a marked increase in size of cytoplasm, nucleoli and nuclei[1], accompanied by a significant increase in DNA content (Fig. 1). In control cultures even the largest nuclei contained 2–4 or only slightly higher DNA amounts, in all exposed cultures none of the large nuclei had 2–4 DNA, but the majority carried a significantly higher DNA content ($P=0.0005$). As can be seen from Table 1 and the example in Fig. 1, this striking increase in DNA was observed very early after exposure (1 day) at a period where mitosis and DNA synthesis were inhibited, and at later periods after exposure (7–45 days), at a period where stimulation of mitosis and DNA synthesis occurred (Table 1, Fig. 1). In addition, from 1–45 days after exposure, all cultures displayed mitotic abnormalities, which were not only more severe, but had also a significantly higher frequency than in control cultures. The abnormal behaviour of chromosomes during division was particularly clear in metaphase and anaphase, in which lagging and breakage of chromosomes and occurrence of tripolar metaphases and very large spindles were observed in living and fixed cultures (Fig. 2*a*–*c*). The difference in frequency of mitotic abnormalities in exposed and control cultures was particularly evident in young cultures. These control cultures had 0–3% abnormal mitosis, and the corresponding exposed cultures had 20–30%, that is a mean increase of about 7 times (Table 1). In older exposed cultures the significantly higher frequency of mitotic abnormalities persisted. Since, however, the frequency of mitotic abnormalities increased with age in controls (up to 10%), the difference, although still being statistically significant, was somewhat less than for young

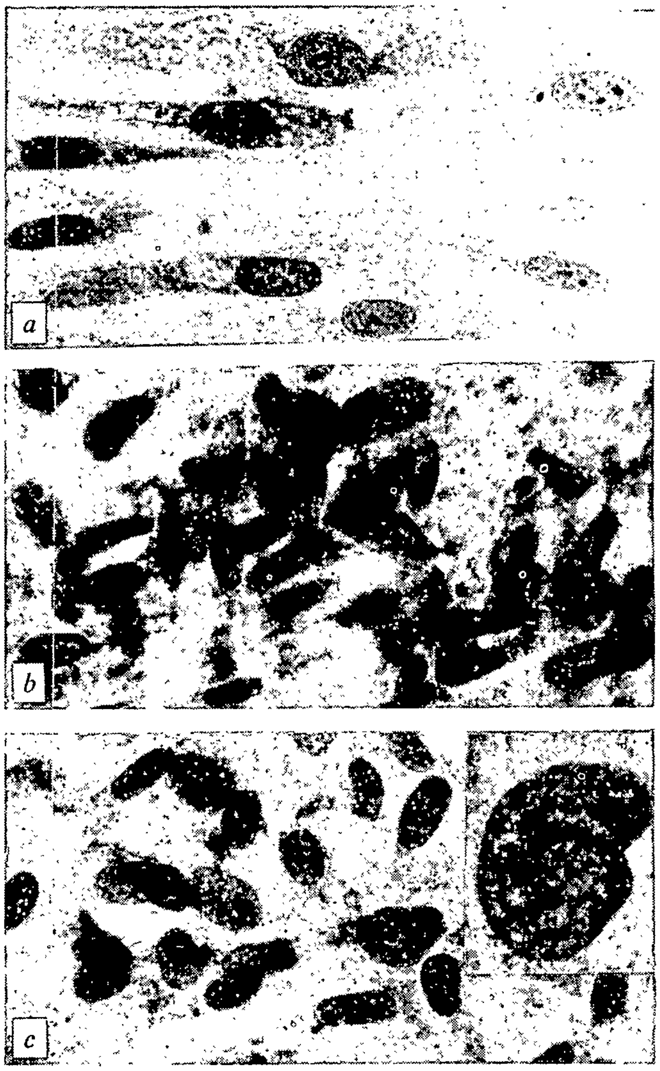


Fig. 3 *a*, Fibroblastic cells in monolayer in control culture of human adult lung explants (H and E, ×500). Note well separated cells. *b*, Same culture as *a*, but 17 days after 4 exposures to 4 puffs of marijuana cigarette smoke (H and E, ×500). Note irregularity and disparity of cells, and criss-cross formation. *c*, Same culture as *a*, 17 days after 4 exposures to 2 puffs of Kentucky Standard cigarette smoke (H and E, ×500). Note essentially the same irregularity of culture as in *b*. Note also irregular shape of large nucleus, multiple nucleoli (inset ×1,000).

Table 1 Comparison of Effects of Fresh Smoke from Marijuana and Kentucky Standard Cigarettes on Mitosis and Metabolism in Fibroblastic Cells of Adult Human Lung Explants ($n_1=200$)

Type of cigarette	Time after last exposure (in days)	Type and mean ratios of frequency of alterations $\frac{\text{exposed cultures}}{\text{controls}}$							
		Mitotic index		DNA synthesis (^{3}H-TdR) (number of labelled cells)		DNA content* (number of cells with high DNA content) $n_2=7{,}500$		Mitotic abnormalities	
		Decrease	Increase	Decrease	Increase	Decrease	Increase	Decrease	Increase
Marijuana	1– 4	4±0.2 pCo=0.001	—	3±0.1 pCo=0.001	—	—	5±0.5 pCo>0.0001	—	7±1.7 pCo>0.0001
	7–45	—	2±0.2 pCo=0.005	—	2±0.2 pCo=0.005	—	5±0.5 pCo>0.0001	—	3±0.6 pCo=0.005
Kentucky Standard whole smoke gas–vapour phase	1– 4	9±0.2 pCo=0.0005	—	10±0.2 pCo>0.0001	—	—	5±0.5 pCo>0.0001	—	7±1.5 pCo>0.0001
	7–45	—	2±0.2 pCo=0.005	—	2±0.2 pCo=0.005	—	5±0.5 pCo>0.0001	—	3±0.5 pCo=0.005

n_1=No. of cultures examined. n_2=No. of cells measured. *Feulgen microspectrography.

cultures (Table 1). A detailed study of time sequential microscopic, ultrastructural and cytochemical effects of marijuana and tobacco smoke on young and old human adult and foetal lung cultures has been completed (Leuchtenberger, C, *et al.*, in preparation).

The marked decrease of DNA synthesis and mitosis observed early after exposure was followed at later periods (7–45 days) by an increase of mitosis and DNA synthesis (Table 1). In comparison with controls there was about a two-fold augmentation of these and this was accompanied by irregular growth, characterized by disparity in shape and size of nuclei and nucleoli, piling up, and criss-cross formations of cells. The appearance of exposed cultures was strikingly different from the corresponding control cultures, which showed rather regular monolayers with more or less contact inhibition (Figs. 3*a–c*).

It therefore seems that fresh smoke from cigarettes made from marijuana evokes essentially the same abnormalities in DNA metabolism, mitosis and growth in fibroblastic cells of human adult lung explants as does whole fresh smoke or the gas-vapour phase from Kentucky Standard cigarettes. This similarity is particularly noteworthy when the important role of cigarette smoke for pulmonary carcinogenesis is examined[5,6], but while it is tempting to suggest that smoke from marijuana cigarettes plays the same role in pulmonary carcinogenesis, no conclusions can be drawn until results of epidemiological studies in human marijuana smokers and chronic inhalation experiments in laboratory animals with marijuana cigarettes become available.

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Effect of Commensal Hydroids on Hermit Crab Competition in the Littoral Zone of Texas

IN Galveston Bay, Texas, the hermit crab *Clibanarius vittatus* is the dominant animal on many shallow mud and sand flats. During the winter the hermits *Pagurus longicarpus* and *Pagurus pollicaris* migrate into the region dominated by *Clibanarius* and remain there until the following spring. Hermit crabs engage in ritualized fights[1] in competition for gastropod shells which are a necessary protection from predators. In both laboratory and field encounters, *Clibanarius* are very aggressive in competition for shells and are usually able to win shell fights with *Pagurus*, even if exceeded in size. As suitable unoccupied shells are extremely rare, *Pagurus* are at a potential disadvantage in competition with *Clibanarius* for this resource.

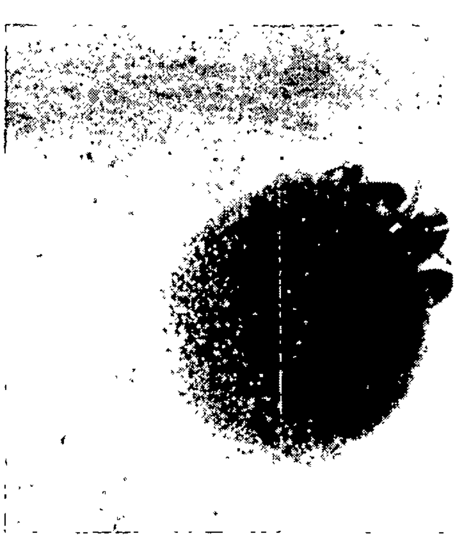

Fig. 1 *Pagurus longicarpus* bearing colonies of *Hydractinia echinata*. Note that any hermit occupying these shells will be in constant contact with the hydroid polyps.

About 20–30% (depending on locality) of *Pagurus* collected bear shells with hydroid colonies, either *Podocoryne carnea* or *Hydractinia echinata* (Fig. 1). These hydrozoan colonies grow on the outside of the shells, secreting an intricate exoskeleton under which the stolons grow and from which the zooids arise. Of several thousand shells occupied by *Clibanarius vittatus*, one bore a healthy colony of commensal hydroids, several had regressing colonies, and others bore skeletal remnants of colonies. (The zooids of both genera of hydroids are readily destroyed by abrasion or other adversities, but living tissue remains in stolons under the skeletal mat. This tissue can regenerate the colony if fed and protected from exposure to air.)

Pagurus spp. usually actively avoid contact with *Clibanarius* in the field. In artificial encounters or when *Clibanarius* are first presented with shells covered with commensal hydroids, *Clibanarius* attempt the normal shell-examination[2] or shell-fighting ritual[1]. When this species contacts the hydroid colony, all types of zooids (gastrozooids, ordinary dactylzooids, and spiral zooids) make the crab behave as if stung. Thereafter, the crab avoids the hydroid-occupied shell as long as it is left in the container. Thus inexperienced *Clibanarius* are repelled by neither visual nor olfactory cues from the hydroid. Repulsion is a result of individual experience. In an early experiment, one of the *Clibanarius*, deprived of its shell, did enter a hydroid-covered shell; but it soon used its heavily armoured chelae to pick off and discard all the zooids it could reach. The hydroids then could not reach the crab.

To demonstrate that *Clibanarius* prefer shells without hydroids, we removed ten *Clibanarius* from their own shells and offered each a shell covered with hydroids (Table 1). Eight of the ten crabs refused to enter the hydroid-covered shells during the 30 min trials. Each of the eight was then offered a clean shell. All eight entered the clean shells. The two crabs which had entered hydroid-covered shells switched to clean shells, one in 2 min 30 s, the other after 45 min. (The hydroids' stings thwarted attempts by the latter crab to leave or to investigate the clean shell.)

To be sure that the hydroid-covered shells were acceptable to crabs after as well as before the tests, twenty *Pagurus* (ten *P. longicarpus* and ten *P. pollicaris*) previously deprived of their shells were then offered the same hydroid-covered shells, and all twenty entered the shells. Only four of the twenty *Pagurus* switched from a hydroid-covered shell to a clean one when given that opportunity. Of these four, two shortly returned to their hydroid-covered shells.

Hydroids were observed to sting neither their *Pagurus* hosts nor other *Pagurus*. *Pagurus* occasionally eat hydroids covering a neighbour's shell. Although such feeding is obviously disadvantageous to the hydroid, it may allow *Pagurus* to become gradually immune in a manner similar to that postulated by Cantacuzene[3] and subsequent authors for acquisition of immunity by *Pagurus prideauxii* to its actinian symbiont *Adamsia palliata*. Alternatively, the hydroid may contain a substance which inhibits its nematocysts from discharging and stinging other members of the colony. An occasional hydroid diet may provide *Pagurus* with such an inhibitor. As *Pagurus* do not aggregate in nature, feeding on hydroids borne by other *Pagurus* does not occur frequently enough to destroy the colonies.

Table 1 Response of Crabs to Shells with and without *Hydractinia echinata* Colonies

Species	Shells with hydroid Trial 1 Accepted by	Time (s)	Shells without hydroid Trial 2*a* Accepted by	Time (s)	Trial 2*b* Accepted by	Time (s)
Clibanarius vittatus	2 of 10	28	8 of 8	19	1 of 2 (see text)	30
Pagurus longicarpus	10 of 10	33			2 of 10	90
Pagurus pollicaris	10 of 10	19			2 of 10 (see text)	20

Each crab was tested individually in a small aquarium. Test was scored as rejection if crab did not enter shell in 30 min. "Time" is mean time from first contact to entrance. "Accepted by" is the number of crabs accepting shell out of the number offered shells. In trial 1, the crab was given shell with hydroid. In trial 2*a*, crabs which rejected hydroid-covered shell in trial 1 were given comparable shell without hydroid. In trial 2*b*, crabs which entered hydroid-covered shell in trial 1 were given comparable shell without hydroid.

Clibanarius with hydroid colonies on the backs of their shells (where the colonies could not sting the crabs) might be protected from losing their shells to other *Clibanarius*. The habits of *Clibanarius vittatus*, however, exclude the hydroids from such an association. At high tide, all three species of crabs studied may be found in water only a few centimetres deep. *Clibanarius* are frequently stranded at low tide, especially when north winds cause tides a metre or more below predicted levels. Both *Pagurus* species avoid exposure by moving to deeper water as the tide recedes. Only once was a straggler observed. The crab had dug a small hole not far from the water line so that its shell protruded only slightly above the water's surface. Even brief exposure to air can cause both hydroid species to drop their zooids. Both *Pagurus* and hydroids die easily on exposure to heat or foul water in the aquarium, while *Clibanarius* in the same containers survive and feed on the dead *Pagurus*. *Pagurus* avoid high temperatures reached in the shallow water of the bay flats (approaching 40° C) by a migration to deeper water during the summer months. Heat, exposure to air, and abrasion caused by the aggregation of large mounds of *Clibanarius* probably account for the dead hydroids found on some of their shells. It is doubtful that a colony could survive long on an inappropriate hermit host such as *Clibanarius vittatus*.

Hydroid colonies in Texas benefit their *Pagurus* hosts by protecting them from *Clibanarius*, and probably from predators —for comparison to *Pagurus bernhardus* see ref. 4. At least in the aquarium, the hydroid receives some food which is dropped by the crab, though the hydroid also catches zooplankton, which may be shared in turn with the crab. The work of Christensen[5] on *Pagurus bernhardus* agrees with these observations, but his work is more extensive and is relevant to the European situation where he worked. Also in the aquarium, and probably in nature, hydroid colonies on shells not occupied by hermits are sometimes smothered by sediments. If a crab carried the shell, both its locomotor activity and respiratory current would help keep the hydroid free of sediment. The association between the hydroids and *Pagurus* spp. is of advantage to both partners, a clear case of true mutualism.

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Epidermal Lesions in Irish Sea Flatfish

PERKINS *et al.*[1] suggest that the apparent increase of epidermal lesions in the flatfish of the north-east Irish Sea during 1971 may be associated with pollutants, particularly polychlorinated biphenyls (PCBs). They suggest that the simultaneous increase of lymphocystis, fin damage and ulcers represents an abnormal situation that may have resulted from the increased dumping operations carried out in the Irish Sea over the past few years.

In April 1972 we completed a similar survey extending over the area from St Bees Head to Liverpool Bay. We also found evidence of lymphocystis in dab, *Limanda limanda*; plaice, *Pleuronectes platessa*; and flounder, *Platichthys flesus*; the infection was restricted to the older fish and this we interpret as increased susceptibility at sexual maturity or, more likely, as a result of the increased number of encounters between fish which takes place during spawning aggregations, thus increasing the chances of transmission. Bacterial ulcers were also observed in these species but were not recorded in another twenty species. Partially and completely healed injuries were observed on the fin margins of the three flatfish species. This damage was almost certainly due to previous capture and subsequent escape from the trawl or rejection by fishermen. We saw no evidence of true fin rot.

The highest incidence of this type of damage occurred in the flounder, the least commercially important and therefore most frequently rejected of all the flatfishes. It is possible that infection had become established in a small number of these damaged fish.

Of 3,468 fish examined, the frequency of infection with lymphocystis in the dab and plaice (1.1 and 1.9% respectively) was similar to that recorded by Perkins *et al.*[1] (1.6 and 1.6%). For these species we found the incidence of ulcers (1.0 and 0.3%) and of fin damage (1.0 and 1.0%) to be significantly less than that recorded in 1971[1] (4.0 and 1.9% for ulcers: 1.9 and 2.3% for fin damage). Of the 397 flounders examined the incidence of lymphocystis, ulcers and fin damage was 14.6, 1.3 and 2.0% respectively, which we could not compare with Perkins's sample of 35 flounders.

If their data represented the coincident peaks of three epizootics in 1971 it seems from our survey that the frequency of fish with ulcers and fin damage declined in 1972. From records gathered by this Ministry during the operation of its scheme for the voluntary control of dumping, there was no corresponding reduction in the quantities of wastes dumped from vessels in this area.

It has been suggested by Brinkmann[2] that a high incidence of epidermal lesions is characteristic of many sea areas where salinity is low and the circulation somewhat restricted. Both lymphocystis and ulcers have been observed in Irish Sea flatfish for over fifty years[3,4], and it is commonly observed by both scientists and fishermen that the frequency of these infections undergoes cyclical fluctuations. Apart from any changes in the virulence of pathogens, these fluctuations are probably related to changes in salinity, water temperature and year-class strength and we believe therefore that, of all the environmental variables which can be invoked to explain these results, pollution is the least likely.

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Courtship-feeding, Egg-size and Breeding Success in Common Terns

Feeding of female birds by their mates is generally known as "courtship-feeding" because it is thought to play a role in establishing and maintaining a pair-bond[1–3]. Its nutritional importance to the female at the time when she is forming eggs has been pointed out[4–8], but no direct evidence for this function has been given.

In the common tern (*Sterna hirundo*)[9–13], as in the closely related Arctic tern (*Sterna paradisaea*)[11–13], courtship takes place in three phases. In the first phase males carry fish around the colony and display to unmated females, but do not feed them regularly until the pair is fairly firmly established. In the second phase the pairs spend much of the daytime on the feeding-grounds, where the male frequently feeds the female; they return to the colony in the evenings. In the third phase the female stays in the pair's territory and is fed there by the male until the clutch is complete. In my study the third phase started between 6 h and 6 days before the first egg was laid. Once settled in the territory, the female spends most of her time there (Fig. 1), leaving it primarily to drink and bathe, catching little or no food for herself.

From May 21 to 28, 1971, I watched twelve pairs of common terns during the third phase of courtship in a colony at Bird Island, Massachusetts, USA (41° 40′ N, 70° 43′ W). Each food item fed to the females was observed from a hide at a range of 2–7 m. Fish (14% of items fed by frequency, 52% by weight) were identified in most cases to species, and their lengths estimated using the birds' bills as templates. Shrimps (48% by weight) could not be identified to species, but were assigned to one of five size-classes. The weight of each food item was estimated from length–weight curves compiled from samples of each species collected near the colony.

Feeding continued for about 14.5 h daily (0430–1900 EST): I watched for the first 9.5 h each day, and made at least two sample watches in each subsequent hour. There were no significant hour-to-hour variations in feeding rate when averaged over the 8-day period, so the 9.5 h samples included about 65% of the food fed to the females. Ranking the males according to the total amount of food brought, the rank order in the incomplete afternoon samples was very similar to that in the systematic morning samples; the latter are used in subsequent comparisons.

Designating the day when the first egg was laid as day L, most females laid their second egg on day $L+2$ and their third egg on day $L+3$ or day $L+4$; two females laid only two eggs. Averaging the data for the twelve pairs, feeding-rates were highest between days $L-2$ and $L+1$, and dropped off sharply after day $L+2$ as the males began to take a share in incubation (Fig. 1). An index of courtship-feeding performance for each pair was obtained by comparing the total biomass fed to the female with the average amount fed to all females on the corresponding days in the laying period. The most complete data were obtained for days $L-2$ to $L+3$ (Fig. 1), but the rank order of the males was not changed significantly by including data for the six pairs observed earlier; accordingly the indices listed in Table 1 are based on data for all days between $L-5$ and $L+3$. The resulting index of courtship-feeding performance was correlated with the total fresh weight of the clutch, and also with the fresh weight of the third egg (assigning zero to the "third egg" in two-egg clutches) (Table 2).

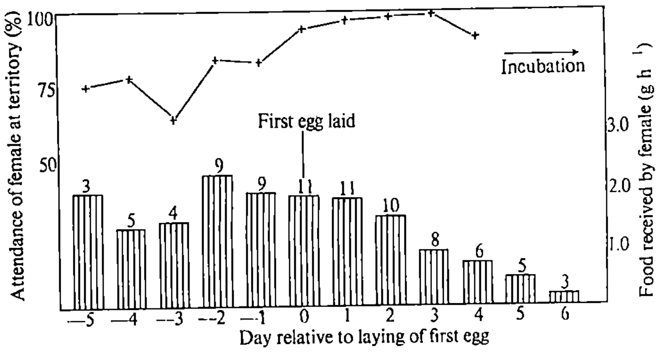

Fig. 1 Mean attendance of females at territory (+—+) and mean rate of feeding of females by males (histograms) during the egg-laying period. Sample sizes (figures above histograms) varied from day to day because of asynchronous laying. Data from females not yet settled (< 60% attendance) are not included.

Altogether thirty-five clutches in the colony were marked and weighed at the time of laying. Chicks were marked at hatching and weighed daily until fledging or death. No eggs or chicks were taken by predators. In most broods chicks from the first two eggs fledged successfully, an exceptionally good performance for the species[14,15]. Of thirty chicks hatched from third eggs ("*C*-chicks"), seven fledged: these hatched from eggs significantly larger than the remaining twenty-three third eggs (Table 2). Of the twelve pairs studied in detail, two fledged their *C*-chicks: these were ranked second and third in the male's courtship-feeding performance, marginally statistically significant ($P=0.089$). Thus fledging success, at least in *C*-chicks in a favourable year, is correlated with egg-size and probably also with the male's performance in courtship-feeding.

In a 1972 egg-exchange experiment, *C*-chicks hatched from large eggs survived much better than those from small eggs during their first four days of life, even when raised by parents that had laid small eggs. A similar result has been reported for herring gulls (*Larus argentatus*)[16]. In common terns, unlike herring gulls[16], neither large eggs nor the large chicks that hatch from them appear to contain significantly more energy reserves in the form of lipids than small eggs or chicks (R. W. Risebrough and M. Gilbertson, unpublished data), but large chicks appear more vigorous than small chicks in competing for food with their older siblings; this might explain their better early survival in a year when food is short at the time of hatching. However, in 1971 only one *C*-chick died before the age of four days; most of the deaths occurred at ages of 8–13 days, when survival is expected to depend less on initial weight and vigour and more on subsequent parental care.

In nine pairs, including seven of the twelve studied during courtship, one of the parents was marked, and the total amount of food brought to the chicks by each parent was recorded (by the above methods) during at least one complete 24 h period between day $H+1$ and day $H+4$, where H denotes the day when the first egg hatched. At this period the male brings most of the food while the female broods the chicks[12], so the amount of food brought by the male is the most important index of parental feeding. The total weight of the brood on day $H+4$ and the weight of the *C*-chick on its third day of life (usually $H+5$ or $H+6$) were selected as indices of success; by

Table 1 Indices of Breeding Performance for the Twelve Pairs Studied in Detail

Pair	Date of laying first egg	Index of courtship-feeding performance	Total weight of clutch (g)	Weight of third egg (g)	Food fed to chicks by male (g day^{-1})	Weight of brood, day $H+4$ (g)	Weight of *C*-chick, age 3 days (g)	Fledging of *C*-chick
A	May 22	1.47	61.8	20.3	33.1	85.0	13.5	No
B	May 24	1.25	72.5	23.4	62.2	102.0	24.0	Yes
C	May 25	1.24*	63.3	19.8	16.3	76.0	17.5	No
D	May 20	1.19	59.9	19.4	73.7	98.0	22.5	Yes
E	May 28	1.13	63.3	20.3	n.d.	96.5	22.5	No
F	May 25	1.10	43.2	none	n.d.	59.0	—	—
G	May 23	0.86	64.5	21.2	8.0	80.0	10.5	No
H	May 23	0.81	61.7	19.7	26.2	84.5	17.5	No
I	May 27	0.78	59.4	18.6	n.d.	91.0	21.0	No
J	May 26	0.70	56.8	19.6	n.d.	76.5	17.0	No
K	May 21	0.69	61.8	20.1	24.1	75.5	16.5	No
L	May 26	0.63	41.6	none	n.d.	33.5	—	—

* This female, unlike the others, was fed a significant amount of food by other males. Her mate was ranked sixth in the order of food brought by the males; this rank has been used in computing correlations with the feeding, weights, and fledging of the chicks.

n.d., Not studied at this period.

Table 2 Spearman Rank Correlation Coefficients between Indices of Breeding Performance

	Number of pairs	Total weight of clutch	Weight of third egg	Food fed to chicks by male	Weight of brood, day $H+4$	Weight of *C*-chick age 3 days	Fledging of *C*-chick *
Courtship-feeding performance	12	+0.58 †	+0.51 †	+0.57 §	+0.66 †	+0.41 §	§
Total weight of clutch	35		+0.94 ‡	−0.43 ‖	+0.57 ‡	+0.59 ‡	‖
Weight of third egg	32			−0.20 ‖	+0.48 ‡	+0.60 ‡	†
Food fed to chicks by male	9				+0.84 ‡	+0.65 †	†
Weight of brood, day $H+4$	35					+0.65 ‡	‡
Weight of *C*-chick, age 3 days	30						‡

* Mann-Whitney U-test, comparing successful with unsuccessful pairs[19].

‡ $P<0.01$; † $P<0.05$; § $0.05<P<0.1$; ‖ $P>0.1$ (refs. 19, 20). All tests are one-tailed.

these dates the differences in weight between broods are much larger than the initial differences, and primarily reflect differences in growth. These three indices were all positively correlated with courtship-feeding performance and with the fledging success of the *C*-chick, but they were less consistently correlated with egg-size (Table 2).

Survival of *C*-chicks may thus be influenced by the performance of their fathers at two different times: at the time of laying, through the dependence of early survival on egg-size demonstrated in 1972; and in the period after hatching, through the dependence of later survival on parental feeding and early growth (Table 2). The males that performed well at both periods were those that switched most successfully from one group of food species to another: from shrimps and full-grown silversides (*Menidia menidia*) at the time of laying, to silversides fry and cunners (*Tautogolabrus adspersus*) at the time of hatching.

These results suggest a third function for courtship-feeding in common terns, in addition to the two above. The performance of the male in courtship-feeding is a predictor of his future performance in feeding the chicks (Table 2), in the period just after hatching when they are usually most critically dependent on him[12,14,17]. It can thus be used by the female to assess his future performance as a parent. At least until the eggs are fertilized, the female has less time and energy invested in the nesting attempt than the male, and theoretically less to lose by breaking off the courtship if she finds indications of future incompetence[18]. The second phase in courtship could thus be used to test the male's competence in fishing, and the third phase to test his dependability in bringing food to the territory. Although I obtained no conclusive evidence that pairs broke up during these phases in courtship, I saw several females which settled in my study-plot for one or two days, but moved away after receiving relatively little food from their putative mates. During the first phase, incipient pairs break up very frequently, as both males and females display to a number of potential mates[9–13]. The male's use of a fish in his advertising flights at this period may have more than symbolic significance: it indicates his future potential as a provider at the time when females are actively selecting their mates.

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BOOK REVIEWS

Science in an Eccentric Mirror

Science at the Crossroads. By Herbert Dingle. Pp. 256. (Martin, Brian and O'Keefe: London, September 1972.) £3.

THIS is Professor Dingle's account of his attempt to persuade the scientific community that the theory of relativity is wrong and should be repudiated. It is a singular, idiosyncratic, and in many ways outrageous book, but should not be dismissed as altogether worthless. The image that science presents to its experienced practitioners is well-rounded and almost without blemish; a reflexion of ourselves from a cracked and eccentric mirror may sometimes be healthy.

Professor Dingle's quixotic quest is for a valid answer to what he calls "the question". "According to the special relativity theory, as expounded by Einstein in his original paper, two similar, regularly running clocks, A and B, in uniform relative motion, must work at different rates. In mathematical terms, the intervals dt and dt', which they record between the same two events. are related by the Lorentz transformation, according to which $dt \neq dt'$. Hence one clock must work steadily at a slower rate than the other. The theory, however, provides no indication of which clock that is, and the question inevitably arises: how is the slower-working clock distinguished?"

This is a perfectly reasonable question to which science should indeed give an answer. But first, what do we mean by "science" in this context? Professor Dingle strove mightily, by the magic of his pen, to charm such an answer from such high and mighty figures as the editor of *Nature* and several successive presidents of the Royal Society. But physics has no Pope with authority to proclaim doctrine. Several experts on relativity — especially Professor McRae—made reasoned replies demonstrating the fallacies in Dingle's objections; but he claimed that these were inadequate, or that they were formulated in mysterious mathematical language which did not correspond to any genuine physical reality. The fact that other experts were reluctant to enter the lists against him was interpreted as a cowardly conspiracy of silence, symptomatic of a state of decadence in the intellectual integrity of science.

The charge of mathematical mystification is not altogether unjustified. Those theoretical physicists who discuss tachyons as if they were as familiar as boiled eggs, and assert the metaphysical principle "anything which is not prohibited is compulsory", deserve several bucketfuls of cold scepticism. The whole structure of modern physics is such a composite of mathematical theory and sophisticated observation that one is often at a loss to know whether any particular statement is logically necessary but empirically false or experimentally verified but theoretically anomalous. But never forget, oh best beloved, the positron, the neutrino, parity non-conservation, and the omega-minus, which were predicted in this spirit and subsequently observed.

He is also quite justified in expecting the professional experts to provide answers, if they can, to all questions concerning their specialties. Scientific knowledge is no more than what scientists know, and what they agree, one with another, to be the truth of the matter. Relativity theory is the responsibility of the relativists, in the first instance, and they cannot decline the challenge of debate, however sure they may be of their ground. In default of such champions, physicists generally must be willing to take up the cause, and at least reassure themselves, by public discussion, that their conventional opinions are soundly based. The scientific community has no machinery for delegating this responsibility to particular individuals. Professor Dingle's suspicions would be rightly inflamed if there had, as he claims, been an inadequate public reply to his objections.

But here, again, he is grossly unfair. The clock paradox, and its resolution, was discussed in detail by Einstein himself, and by many later scholars. Glancing at my own bookshelf, I find Pauli's admirable treatise on Relativity Theory (originally published in 1921) which explains the position very clearly, and *Introducing Relativity* by W. G. V. Rosser, published in 1967, which devotes about 50 pages to this very topic, with particular reference to Dingle's arguments. In the library there is *Time and the Space Traveller*, by L. Marder (1971), which is entirely concerned with the theoretical analysis and experimental confirmation of relativistic time phenomena. Books such as these have been favourably reviewed, recommended as textbooks, and made the basis for undergraduate lectures in every university in the country. They have been worked over carefully without adverse comment by a large number of theoretical and experimental physicists who have been thoroughly alerted by one or another of Professor Dingle's numerous communications. In a community where honesty, integrity and mordant self-criticism are the norms of intellectual activity, this is as much of an answer as he can reasonably expect. The fact that he, one man in a thousand, thinks differently is scarcely a major flaw in the scientific consensus.

Yet there is always the necessity to doubt. Looking at the previous paragraph, I thought of another crank, Alfred Wegener, and of the geology textbooks that rejected continental drift for half a century. He, too, wrote some easily refuted nonsense in places on which the experts could happily pounce. The deeper and more secure our beliefs, the more difficulty and the greater the necessity for occasionally holding it possible that we are mistaken. I must say that I should rather like a simple but accurate answer to Professor Dingle's "question"—not at the level of showing up the elementary fallacies which he spins around it but as a serious issue of natural philosophy.

Not being active in research or teaching in this field, I can speak with little authority, but I would interpret the present position somewhat along the following lines. (*a*) Experiment has amply confirmed that rapidly moving "clocks" (for example, radioactively decaying particles) seem to run slow as seen by a stationary observer. (*b*) Observers in different frames moving relative to one another would certainly disagree about whose clocks seemed to be running the faster. But special relativity cannot resolve the disagreement because it deals only with clocks (or assemblies of clocks or "observers" or coordinate frames) that are moving relative to one another with uniform velocity; clocks that have come close to one another at one instant of their respective careers can never come together again to check for disynchrony. (*c*) To make this comparison, the clocks must be accelerated (or decelerated) relative to one another according to some scheme that will bring them back into the same ball park. Each clock can then yield a number recording the interval of time between the two events of their initial and final meeting. (*d*) These two numbers need not be the same. The interval recorded by each clock depends upon its dynamical history between the two events. If their histories are not the same, then one clock will be found to have run more slowly than the other. This has been confirmed experimentally by taking an atomic clock around the world in a jet plane. (*e*) To distinguish the slower-working clock (as demanded by Professor Dingle) one must use the theory of *general* relativity, which takes account of accelerations. The dynamical history of a clock is represented geometrically by its world line in "space-time". A clock is itself, by definition, a physical system that integrates infinitesimal intervals, ds, along its world line. The axioms of the tensor calculus ensure that such an integral is well defined, and not arbitrarily dependent on the notion of an observer. But the integrated interval is not the same along every world line between two events. (Similarly, the distance from Bristol to London along the M4 is a well defined quantity, but it is not the same as the mileage that would be recorded in going up the M5 to Birmingham and then down the M1 to London.) (*f*) To avoid the use of this difficult mathematical language, one must introduce the "physical" concept of a gravitational field—a "fictitious" field of force observed by a physicist who does not realize that he is being accelerated. The simpler consequences of general relativity for the measurement of time can then be deduced phenomenologically from the principle that "a clock runs more slowly in a region of high gravitational potential". In the case of the elementary "twin paradox", for example, the chap that has felt the accelerations and decelerations of the rocket flight to alpha-Centauri has aged less than his brother left on Earth, because his gravitational potential seems to himself much higher throughout the flight. (*g*) In fact, the answer to Dingle's "question" is simple: the fastest working clock between any two events is one that travels between them by free fall. (*h*) Hypothetical or actual experiments involving the synchronization of clocks are thus not in contradiction with the principle of relativity; they tell us nothing special about the velocity of light, the motion of the ether, absolute scales of time, or other ingredients of non-relativistic theories of space and time. Nor is there any evidence that our present ways of thinking about these things pose a greater danger for mankind (as Dingle asserts) than do any of our other cock-eyed, makeshift, ramshackle theories of the physical world. Interesting, subtle, and controversial questions arise when we try to think about the space–time metric of the whole cosmos, or set down the equations of physics near a "black hole"—but that was in another country: and besides (if we are to believe Dingle) the wench is dead.

For one reader, at least, this book has proved not altogether worthless. In its foolish, sincere, dishonest, wrongheaded, exasperatingly charming way, it has made me think further about the way in which "scientific knowledge" is validated, affirmed and made manifest in modern society, and about the foundations for my belief in the relativistic theory of space, time and gravitation. The fact that it has strengthened my confidence in the conventional wisdom at both levels need not be an objection to other people going through this same process. JOHN ZIMAN

Statistical Mechanics

Statistical Mechanics. By R. K. Pathria. Pp. xiii+527. (Pergamon: Oxford and New York, September 1972.) £8.

IT is not, I hope, my most original remark to observe that the universe of knowledge is in a process of rapid expansion. The reason for this observation here is that the subject of statistical mechanics presents rather a good illustration. Just before the war, and into the 1950s, one had in Fowler's *Statistical Mechanics* a standard treatise. More up-to-date books at various levels of distinction and coverage were written as the subject attracted growing attention from physicists, chemists and also mathematicians, and Fowler's book is no longer a standard reference. Nonetheless, it is good to see that it appears in the bibliography of the book under review, together with the books by T. L. Hill, K. Huang, A. Munster, R. Kubo and others. The time of a single standard reference in statistical mechanics has clearly passed for ever. Instead, the group of best books continues to grow. It is (fortunately) not exactly my task to place such books on some kind of ranking list. Suffice it to say, therefore, that the book under review belongs to this top group.

To any colleague who regularly reads the publications of the Hindustan Publishing Corporation of Delhi, this observation will come as no surprise. He will have noted (on their 1963 list) Pathria's first book on the theory of relativity, and will have observed that it attained a high level of clarity in the exposition of a difficult topic. Pathria's text on statistical mechanics has the same quality. It is careful, clear, offers many problems at the end of sections, and shows the author to be a wide reader who will refer from time to time to important or interesting topics which are sometimes left out of statistical mechanics texts. The theory of rotons, Chandresekhar's limit and temperature-dependent energy levels are just a few examples. True, he has 507 pages on which to do so, but with this number of pages it is hardly the most voluminous book on statistical mechanics—a subject well known to resemble dialectical materialism in the size of volumes devoted to its study.

To indicate coverage: chapters 1 to 8 treat foundations and applications to ideal systems. Clusters, pseudo-potentials and second quantization as means of treating interacting systems follow in chapters 9 to 11. The concluding chapters deal with phase transitions, including a three page introduction to critical indices, and fluctuations.

The book contains rather little on the solid state or on melting apart from thermionic emission and the Debye theory, and not much on more chemical topics like mass action laws or reaction kinetics, though one problem is devoted to the Debye-Hückel theory of electrolytes. This is no criticism; authors must make selections. It would be unexpected and unlikely that this is the one occasion when the reviewer and the book are matched ideally, and there are accordingly some criticisms. The author's reference to Kappler 1931 for the study of the mean square deflexion of a galvanometer needle is rather old when the work of R. V. Jones and C. W. McCombie (in *Phil. Trans. Roy. Soc.* of 1952) is available, and I felt it to be a pity that his remarks about such basic questions as detailed balance and master equations were so brief, and almost incidental.

Returning now to the citation of Fowler's book, this appears with a publication date of 1955, whereas the last (second) edition was in fact published in 1936. It would, I think, be desirable if at an appropriate international convention it were agreed that books which are reprinted should be cited in a bibliography not with the date of the reprint but with the date of the original publication. A citation giving a much later date of a reprint could be highly misleading.

Lastly, in his treatment of mass motion, after maximizing the entropy with Lagrangian multipliers α, β, γ for the moving system, the author assumes (top of page 153) that $\beta=1/kT$, thus introducing the temperature of a moving object. From this essential step then follows the temperature transformation $T=T_0\sqrt{(1-v^2/c^2)}$. Most readers will not spot that this is the crucial step in Pathria's argument (which, in fact, I would not regard as unique and would prefer not to make at all), and it would have been worthy of a separate caution. In fact, it can be shown that if one assumes that thermodynamic relations are Lorentz-invariant then this temperature transformation follows. It would therefore have been sensible in such a discussion to raise the question of the Lorentz invariance of thermodynamic relations in the first place. Nonetheless, I believe that this is an excellent book from which to learn the methods and results of statistical mechanics. P. T. LANDSBERG

Ecological Personalities

Philosophers of the Earth; Conversations with Ecologists. By Ann Chisholm. Pp. 201. (Sidgwick and Jackson.) £2.50.

ANY period of history, as observed by those living at the time, is coloured not only by the events that make up that period of history but also by the state of development that those events had reached when the observer first became aware of them. A sense of history and an awareness of the importance and relevance of the events that preceded those being observed is a necessary prerequisite if the full significance of the new events and the contribution being made by the players in these events is to be understood. Without these prerequisites the records made by an observer living through the period of history in question will suffer from distortion and be highly subjective. A journalist when reporting an event for the impermanent column of a newspaper may up to a point be excused this background, but when he or she records in the permanent form of the book then, like the historian, he or she must try to see his or her heroes and the events they are influencing in a more critical light.

Miss Chisholm informs us in her foreword that she became aware of the word "ecology", and I assume the concomitant "environmental or ecological crisis", in the autumn of 1969 just before Sir Frank Fraser Darling's Reith Lectures on the BBC. This is somewhat surprising as the "crisis" had been news off and on for at least 10 years by that time and had reached an all-time peak during 1967 when the Torrey Canyon went ashore; however, it does explain her selection of "heroes", or what she calls Earth philosophers, and strange bedfellows some of them make. She is clearly influenced by the state the "environmental movement" had reached and by the personalities that occupied the centre of the stage at the moment that she became aware of it, but she has had the good sense to take advice and seek out some of those whose contribution, although no less important than that of the more popular figures, is perhaps less public. Each of us would, I am sure, have selected a different bunch of personalities but we would have had to include at least half of those interviewed in this book if we were to provide a critical review of the "environmental movement" of the past decade.

Unfortunately Miss Chisholm seems less aware of, or perhaps less interested in, the events themselves. She seems less informed about the events that preceded her awakening and incidentally that of many millions of other people too. For example, in the third paragraph of her foreword the author says "In America, as usual several steps ahead. . . ." Really? This is indicative of the sort of thing I referred to in my first paragraph. There is no doubt that the recent response of the USA to environmental wrongs has been significant but it has been a long time coming. Some of the countries in Europe have been doing things too and for longer. Where credit is due give it, but don't hand out laurels where they are not deserved.

However, Miss Chisholm's selection of heroes is interesting; some, as she admits, are not ecologists, in spite of the book's subtitle *Conversations with Ecologists,* but most of them have made major contributions to "environmental thinking". This use, or rather misuse, of the word "ecology" is one of the things troubling the real ecologists; it is rapidly becoming a debased word along with "environment", a situation which does nothing but add to the mounting difficulties facing the world community, and the journalists must take some of the responsibility for this debasement and the resulting confusion.

Miss Chisholm writes in a nice easy style but the question does arise in my mind, for whom does she write? If the layman is sufficiently interested in the "environmental movement" to want to know something of the characters involved, then all well and good, but I doubt whether the "environmentalists" or "ecologists", using the non-debased forms, will find much in the *Philosophers of the Earth* to interest them. The treatment of necessity is too superficial and for the same reason the book will not be of much use to the historian —the absence of an index in any case makes the book next to useless for the researcher. Perhaps the author would have been better advised to select fewer and to delve deeper. In any event she has spared us yet another book on the "environmental crisis" but has focused on some of the personalities involved in the major events that historians will consider a revolutionary period of history. ARTHUR BOURNE

Research Directory

Scientific Research in British Universities and Colleges, 1971–72, compiled by the Department of Education and Science. Vol. I: *Physical Sciences.* Pp. xxi+924. Vol. II: *Biological Sciences.* Pp. xxi+769. Vol. III: *Social Sciences (including Government Departments and Other Institutions).* Pp. xxix+690. (Her Majesty's Stationery Office: London, 1972.) Vol. I £6.50. Vol. II £6. Vol. III £5.50.

THE 1971-72 edition of *Scientific Research in British Universities and Colleges* is still larger and more comprehensive than the previous issues. It is a unique and valuable work of reference, giving a nearly complete guide to current academic scientific and technical research. In addition, the Social Sciences volume covers research in Government and some other institutions, and this year includes Economic and Social History as a new subject heading.

The full subject and name indices enable the user to gain a fair indication of the scope of the research effort in any particular field, or to discover the current research interests of a particular department or individual. Every research worker should be familiar with it; those who are responsible for the organization or financing of scientific research cannot afford to be without it. It gives an overall view without which any research policy will be ill-informed and consequently misconceived.

I am aware of the enormous effort that must go into the publishing of this work, and would like to pay tribute to the compilers in the Office for Scientific and Technical Information; but now that it has grown so large, perhaps it is time for them to reconsider the scope and presentation of this work. What was suitable for the small, single-volume older editions is not really suitable to the present massive compilation. Faults or defects which were then not too serious are now more obvious and can present more difficulties to the user.

It is doubtful whether the separation

of subjects into three overlapping volumes is an advantage. It should be possible to present all the information in a more compact, yet still legible, form. Every relevant department, and, as far as possible, every individual should appear, with a clear indication of the main research interests of each person. The subject index is badly in need of improvement, perhaps by controlling the main index terms and greatly increasing the amount of cross-indexing. This presents great difficulties, but the compilers are in the Office for Scientific and Technical Information and might therefore be expected to do a little better. The present indices are somewhat lacking in both precision and accuracy.

Perhaps most important of all is a change in our attitude to works of this kind. All research workers (security considerations excepted) should consider it essential that details of their work should appear in the key directories. Those who finance their work might consider making this a condition of their grants. Only then will we have easy access to the facts we need to answer the many questions being raised today about the direction and utility of scientific research.

JEREMY WESTON

Experimental Prebiology

Origins of Life. By Cyril Ponnamperuma. Pp. 215+150 illustrations, 20 in full colour. (Thames and Hudson: London, October 1972.) £2.25 cloth; £1.25 paper.

This stands out among the welter of recent books on the origin of life by being the smallest and best illustrated to appear. It is a book designed for the non-specialist, and it is a pleasure to welcome it as a conspicuous success. Ponnamperuma, speaking with the full authority of one of the world's foremost practitioners in the field of experimental prebiology, has nevertheless been able to express himself in language that is readily comprehensible to the non-chemist. For many years he was with NASA in the exobiology division; he is now at the University of Maryland as director of the laboratory of chemical evolution.

Ten of the sixteen chapters are devoted to aspects of chemical evolution, and it is refreshing to read not only of the successes of the past, but also of plans for future experimentation. The other six chapters comprehend investigations of meteorites, and deal with other aspects of exobiology. Some of these chapters are highly speculative, and almost escape the boundaries of science. Perhaps there are better accounts to be found elsewhere dealing with the fossil evidence, and with the possibility of intelligent life beyond the Earth. But there is no better account of the way that experimentation has illumined the processes of chemical evolution and our search for the origin of life.

The munificence of the illustrations can only be rivalled by other Thames and Hudson books in the same series. Chosen not by the author but by the publishers, they vary in relevance, and though they add much to the pleasure and interest of the volume, some are so inappropriate as to be misleading. What possible excuse can be found, for example, for illustrating a prebiotic site for the origin of life with a picture of the luxuriant vegetation of a tropical lagoon?

P. C. SYLVESTER-BRADLEY

Organophosphorus

Organophosphorus Chemistry. By B. J. Walker. Pp. 278. (Penguin: Harmondsworth, Middlesex, October 1972.) £3.

As a subject like organophosphorus chemistry grows, and itself begins to divide into specialisms—and to disappear into the decent obscurity of specialist journals—the single volume text becomes more than ever indispensable. Dr Walker's book is aimed at the interested graduate student and the final year graduate (may his tribe increase) who is taking organophosphorus chemistry as a special topic and has £3 to spend.

To cover so broad a field in so small a space an author must have very clear ideas on what to leave out, and here Dr Walker's judgment is sound. He provides a competent mechanistic treatment of the most important areas, at the expense of any systematic approach to synthesis in this field. There is a good account of the use of various spectroscopic methods in *Organophosphorus Chemistry,* and extended coverage of two topics which are clearly of special importance. These are the Wittig reaction, where the author is expert and produces an excellent review, and phosphorus in biological processes, where he is not. This last is the weakest chapter in the book, and ranges over biological energy transfer and the structures of DNA and the various RNAs (including a reference to something called the codon), without any real attempt to relate them to the organophosphorus chemistry involved.

The author also falls foul of SI units. He gives bond lengths in metres, but the molecules unfortunately come out only one tenth of the usual size. After page 141 Angstrom units appear, with a correct length in metres given also; with the curious result that the P–C bond in ylids appears to be ten times longer than all the other bonds in the molecule. These are not typical, however, of a book which is fairly free of typographical errors and is attractively printed and produced. Sets of examples appear at the ends of chapters, and the bibliography is a model for any author, organized by topic, with a helpful brief description of each reference cited. The book can be recommended to the students for whom it is intended, and to libraries catering for them.

A. J. KIRBY

Chemical Lists

Chemical Substructure Index 1971. Annual Cumulative Edition. Part 1: Substructure Index A–Q, Users' Guide. Part 2: Substructure Index Q–9Y, Peptides. (Institute for Scientific Information: Pennsylvania and Uxbridge, Middlesex 1972.) N.p.

In his searches for information from secondary journals, the average chemist depends largely on *Chemical Abstracts* with its wide area of coverage and its various indexes. But these virtues carry a penalty difficult to avoid—the time interval between publication in a primary journal and the appearance of the corresponding abstract.

To reduce this interval for some journals, the Institute for Scientific Information publishes *Current Abstracts of Chemistry* and *Index Chemicus.* It also provides other aids based on the same material, including computer tapes, programs, and printed lists, enabling information services of varying degrees of complexity to be set up by users themselves, according to their needs. One of these aids consists of a listing of all chemical compounds enumerated in *Current Abstracts of Chemistry,* the *Chemical Substructure Index* (*CSI*), which is produced monthly and cumulated annually to give the volumes under review.

The compounds are encoded into the Wiswesser Line Notation (WLN) and then listed alphanumerically in a permuted form under each significant symbol. There is also a "Quikscan" feature which indicates the presence of such symbols, although not their order. From this information, individual compounds or many part structures may be identified. In an attempt to ensure that search methods used will be correct, the listing is preceded by the notations for "Frequently Found Substructures", and by a *CSI Users' Guide.*

The encoders have produced notations of a good standard, and settle any problems arising in this connexion with WLN experts in the Chemical Notation Association, so that adverse criticism of the listing itself is not justified.

The preceding dictionary of substructures and the guide for users are in a very different category, however. Many of the notations in the dictionary are misleading or inaccurate. There is no indication as to which way a group is written to start a notation. One way of denoting an isothiocyano group and the notation for any azoxy group are incorrect, although only the correct form appears in the subsequent index. Some alternative ways of denoting branched structures are omitted.

The *Users' Guide* also depicts a situation which does not exist in the main index. Some examples of listings are shown lacking alphabetization after the initial grouping, and a wrong notation appears in one section.

Most of these errors do not affect the main body of the work, and probably indicate no more than that a thorough overhaul of the *Guide* is long overdue. But they do show how wrong it would be to attempt to use non-technical effort for search procedures, even though this is recommended by the *Guide*. The problems could be largely avoided by the use of WLN expertise, if only of a minor order, and this would avoid answers which result in an unjustifiable lack of confidence in the whole method. Considering how admirable the objectives behind the production of these volumes, and how well they are used by some organizations, such a conclusion would be as regrettable as it would be false.

P. A. BAKER

Insect Enthusiasts

American Entomologists. By Arnold Mallis. Pp. xiv+549. (Rutgers University: New Brunswick, New Jersey, October 1971.) $15.

THIS book contains biographical accounts and photographs of 206 entomologists of the United States and Canada. The subjects are roughly classified according to their spheres of interest. Among the pioneer entomologists the name of Thomas Say (1787–1834) is well known from the number of species he named and described. He was a great traveller and collector. T. W. Harris (1795–1856) combined systematic entomology with advice to farmers on the new pests they were continually discovering—all as the spare-time job of a conscientious and over-driven librarian at Harvard. It is remarkable how many later entomologists were inspired by his *Insects Injurious to Vegetation*. The first of the professional state entomologists was Asa Fitch (1809–1879) appointed by the New York State Legislature in 1854 to produce a long series of reports on noxious, beneficial and other insects in the state of New York. "I sometimes think," he wrote, "that there is no kind of mischief going on in the world of nature around us but that there is some insect at the bottom of it." Thomas Glover (1813–1883) was the first federal entomologist, appointed in the Bureau of Agriculture in 1854. He was succeeded in 1878 by that colourful figure C. V. Riley (1843–1893): a gifted entomologist, wholly self-taught, intensely self-reliant, producing detailed descriptions of life histories, devising new methods of control and building an organization that was to become a most successful undertaking. His life has been well documented from many sources: his ambition and self-aggrandizement, his habit, like many others of the time, of appropriating the discoveries of his juniors, were well known—but failed to obscure his tremendous accomplishments.

L. O. Howard (1857–1950), whom many of us remember well, was brought up in this difficult school and has given a racy and good humoured account of it. He succeeded Riley at the age of thirty-seven in 1894; and under him the Bureau of Entomology came to maturity and the stature of the applied entomologist in the United States rose to a level that is difficult for us in Great Britain to appreciate. Howard was trained under J. H. Comstock (1849–1931) who had been more or less orphaned at the age of four, had very little schooling and a severe impediment in his speech; but after discovering Harris's *Insects Injurious to Vegetation* he developed a passion for entomology. Under pressure from his student contemporaries the college authorities permitted him to give a course in entomology in his sophomore year at Cornell—where he remained for sixty years and built up the leading teaching centre for entomologists in the United States.

Comstock is classified as a notable teacher; and so is E. O. Essig (1884–1964). Essig worked his way through college and became a brilliant and popular teacher. He was devoted to California—as one who accompanied him through the forests of the High Sierra could not fail to appreciate. He wrote a *History of Entomology* in 1931 with over one thousand pages—which referred to nothing outside California! But one learns in this book that the publishers were responsible for omitting the words "*in California*". It may be that Essig did not see much difference. G. F. Ferris (1893–1958) and R. E. Snodgrass (1875–1962) also appear as notable teachers. The students of Snodgrass are, of course, the entomologists of the world. He had a chequered career at the outset, losing appointments in entomology it would seem by reason of a propensity for practical joking; and was forced to take up commercial illustrating and odd jobs, until he was hired by L. O. Howard and given a post, primarily as an illustrator, in the Bureau of Entomology. There he remained for most of his life, devoting most of his time to insect morphology—a strange official anomaly for which we may be eternally grateful to L. O. Howard. He was not always tied to the microscope; I remember him as a splendid guide in the woods of Maryland.

So the story continues. A most fascinating book for entomologists to dip into. Some subjects, of course, are better documented than others. G. C. Crampton (1881–1951) is underestimated. A curious omission is the name of W. T. M. Forbes of Cornell, who was publishing extensively at the beginning of the century; but being still alive he did not qualify for entry when this book went to press.

V. B. WIGGLESWORTH

Dental Scrapbook

Dental Morphology and Evolution. Edited by A. A. Dahlberg. Pp. x+350. (Chicago University: Chicago and London, 1972.) £9.

PROFESSOR DAHLBERG has ably edited this volume and has provided his own fulsome review as the introduction. I must confess to a certain unease about this book in view of some of the extravagant claims made for it. Perhaps the strongest impression was the sense of *déjà vu*. Much of the work included has been overtaken by events. There have been a number of major symposia and books on comparable topics in the last few years most of which are more up to date than Dahlberg's.

The reason is not far to seek. The papers published in *Dental Morphology and Evolution* were delivered at a symposium in 1968; they reached me in the summer of 1972. Such an unconscionable delay in publishing has rendered what might have been a valuable contribution in 1969 significantly less so in 1972. Advances in the study of teeth move too fast for such a delay to be tolerable. The publishers have rendered a disservice to the authors, some of whom are understandably bitter over this delay. Indeed one author has vouchsafed the intelligence that his paper should not have been published now!

The articles by Turnbull and Clemens have been overtaken by the *Linnean Society Symposium (1970) on Early Mammals* (published 1971). Likewise the paper by Hiiemae and Crompton is the precursor of the major contribution by the same authors submitted for publication in 1969 and published in 1970.

The electron-scanning microscope study by Boyde entitled "Comparative Histology of Mammalian Teeth" is interesting as far as it goes but it does not go very far. Alan Boyde's flood of further work renders this contribution something of an aperitif after the meal. Likewise, Poole's "Introduction to the Phylogeny of Calcified Tissues" has been dealt with by other authors (including Poole himself) in greater depth elsewhere. The impression is given that it was a précis of the major papers of Orvig and Poole published in 1967.

Papers 12, 13, 14, 15 and 16 seem to have little significant contribution to make. Hershkovitz's attempt at a new dental morphological terminology is valiant but by its very nature doomed. Something must be done sometime, but yet another plethora of cumbersome terms simply perpetuates the appalling reputation that dental "cuspologists" or "cristalogists" have acquired for themselves.

Tonge's review on the role of the mesenchyme in tooth development is welcome and Elwyn Simon's on Oligocene and Miocene Old World Anthropoidae is valuable.

Yes, there are a few good things in this volume and they could have been wholeheartedly welcomed a few years ago.

But even if this volume had appeared as long ago as 1969, it would most probably have received some not over-enthusiastic reviews. The blurb and the introduction read splendidly and are most impressive. The actual contents, in contrast, are a disappointment. This volume is a scrapbook of bits and pieces of varying quality. There is no real link even within the separate sections. Take "Phylogeny" for instance; Turnbull and Clemens have related contributions, the rest bear no relation to each other and precious little to phylogeny. In the final part "Morphology", Dahlberg has contributed an article which discusses the "elusive aspects of dental traits in respect to their penetrance and expressivity"—an apt summary of this volume.

L. B. Halstead

Study of a Scavenger

The Spotted Hyena: a Study of Predation and Social Behaviour. By Hans Kruuk. Pp. xvi+335. (University of Chicago: Chicago and London, 1972.) £6.75.

Because they compete with man, many carnivores are unpopular, the ungainly spotted hyena occupying pride of place as the most despised of all—at least in popular imagination. Even in some recently published general works the picture of a ghastly cowardly scavenger persists. There might seem to be very little to be said in favour of the spotted hyena.

Hans Kruuk, who studied this animal as part of a wider programme of research initiated by the Serengeti Research Institute in Tanzania, has shown how misleading this proverbial image really is. His book is an account of a carefully planned and thoroughly executed research project which will appeal not only to carnivore enthusiasts but also to those concerned with the broader aspects of mammalian ecology; to the palaeontologist; even to the sociologist.

Kruuk left few avenues of investigation unexplored. He observed hyenas by aeroplane and he followed them on the ground both by day and by night. He fired immobilizing drugs and marked representative animals for subsequent re-identification; and he examined their teeth while they were drugged. He fitted a radio transmitter to one hyena and kept it under continuous observation for twelve days; and he studied where the hyenas lived, in one lair becoming covered with fleas in consequence. He studied the relationships of hyenas to one another, to other carnivores and to their prey. He estimated the prevalence of sick prey animals and examined hyena droppings to find out what had been eaten. His wife also took part in the studies, fostering a baby hyena which used the Kruuk house as its den.

The story which emerges—packs of hyenas chasing and killing zebra and wildebeest; lions scavenging from hyenas; and lionesses chased up trees by hyenas—contrasts sharply with established ideas. Perhaps the most important observation is the great adaptability which the spotted hyena is shown to have in relation to its environment. Kruuk found that in the Serengeti National Park hyenas travel great distances in order to keep up with migrating wildebeest with consequent high mortality among cubs left unattended by their mothers. The hyenas in the nearby Ngorongoro caldera, however, were found to be an enclosed sedentary population divided into eight "clans" with clearly defined territories and with lower cub mortality. In contrast to the hunting hyenas of these two areas the hyenas living around the walled town of Harar in Ethiopia have become adapted to a scavenging, almost symbiotic, coexistence with man.

This great adaptability which Kruuk has demonstrated is of far reaching significance. In addition to its more obvious application to animal management in Africa today it opens a new field of study for the palaeontologist with evidence already before him that the spotted hyena once spread to Yorkshire and Ireland, with such varied diet as the interglacial hippopotamus and the woolly mammoth and migratory reindeer of cooler times.

The book is well laid out with clear headings, a good index and a valuable bibliography. There is only one cause for regret. The publishers have bound all the half-tone illustrations together as one signature and have not done full justice to the author's brilliant photographs.

This is a remarkable and important book which will attract a diverse readership.

A. J. Sutcliffe

Purpose in Behaviour

Purposive Explanation in Psychology. By M. Boden. Pp. ix+408. (Harvard University: Cambridge, Massachusetts; Oxford University: London, August 1972.) £6.50.

There has always been a rift in psychology between those who insist that human behaviour can be understood only in purposive terms and those who refuse to acknowledge any but causal-mechanical explanations as scientifically admissible. This book is an attempt to heal that rift by showing us that we can continue in good conscience to be teleologists about human beings, indeed we can scarcely avoid doing so, yet, at the same time, we can recognize that we are physical mechanisms and that ultimately all psychological phenomena are caused by brain processes. The author introduces a valuable distinction here between "strict reducibility" which would imply that all the concepts which appear in the one language must be translatable into those belonging to the other language, so that the former is, in the last resort, redundant, and "empirical reducibility" which requires only the possibility of there being bridging laws which put the two in correspondence. It is this latter benign kind of reductionism which, according to the author, obtains between psychology and physiology. Much of her book is devoted to a detailed examination of the psychology of William McDougall who, though not much read these days, remains historically the arch-spokesman of the teleological approach in psychology. She defends her thesis by showing that, contrary to what McDougall himself believed, his approach was not incompatible with an empirical reductionism. She supports this by appealing at length to the new science of artificial intelligence where the same dichotomy reappears as between the purposive aspects of the programming and the deterministic aspects of its physical embodiment in an electronic machine.

The book is a powerfully argued and welcome contribution to the growing body of literature of recent years dealing with the philosophical foundations of psychology. However, the author's treatment of the mind–body problem which was so central for McDougall is, I think, marred by certain philosophical preconceptions which prevent her from doing justice to the dualist-interactionist position. John Beloff

INSTRUMENT REVIEW

Laser Velocity Measurements

Laser Interferometer 3SLVI-204 (Systems, Science and Software), from £3,300.

EVER since Newton discovered the interference rings which bear his name, optical interferometers have been used to measure optical distances by fringe counting. Until the 1960s these interferometers were used with conventional light sources, and all suffered from the short coherence length of the light, which meant that only small path differences (up to 30 cm) between the two component beams of the interferometer could be measured. This distance is estimated from the line width of the source (0.01 Å).

The introduction of lasers, with line widths a factor $\sim 10^{10}$ smaller, increased the coherence length to many kilometres and enlarged the path difference that can be used in an interferometer to the same distance. For example, an interferometer (Fig. 1*a*) may be used to measure a change in position of a distant reflector by counting fringes in the combined beam. The instrument is commonly known as a displacement interferometer and produces a fringe change of $2s/\lambda$ where s is the distance moved by the reflector. Velocity can also be measured with this instrument by measuring the rate at which fringes move across the detector. Currently available amplifying and recording equipment, however, limits the fringe rate that can be handled to ~100 MHz and in consequence limits the velocity that can be measured to ~ 0.03 mm μs^{-1}.

To overcome this limitation Barker (*Fine Structure and Release Wave Shapes in Aluminium by the Velocity Interferometer Technique,* SC–DC–66–2447 (Sandia Laboratory, Albuquerque, New Mexico, 1966)) has suggested that using the Doppler effect an interferometer could be made to measure velocity directly by splitting the returned beam from the reflector and combining it again with one component delayed (Fig. 1*b*). Then the fringe change between two states of constant velocity is $2\,lv/\lambda c$, where l is the delay leg length, c the velocity of light and v the change in reflector velocity. The quantity $(\lambda c/2l)$ is the fringe constant, conveniently measured in units of mm μs^{-1} fringe^{-1}. This instrument is commonly known as a velocity interferometer, but it is as well to note that the quantity measured by the instrument is not exactly velocity; Clifton (*J. Appl. Phys.*, **41**, 5335 ; 1970) has discussed the approximations involved. There is no limit to the maximum velocity that can be measured, for, in practice, the delay leg can be made as short as is required. The lower limit, set by the fact that a long delay leg is required for small fringe constants, may necessitate separate mounting of the reflector prism, and shake in the return beam caused by floor vibration can be excessive. Any user contemplating a velocity interferometer with a fringe constant less than 0.01 mm μs^{-1} fringe^{-1} should consider isolating both interferometer and reflector prism from floor vibration. Alternatively, if slightly larger fringe constants can be used, it is our experience that the optical path of the delay leg can be folded within the base of the interferometer using an extra prism. No special isolation from vibration is necessary for this folded delay leg or indeed for a normal interferometer mounted on a single platform. Target shake induced by floor vibration is not important in a velocity interferometer, but may be troublesome in a displacement interferometer.

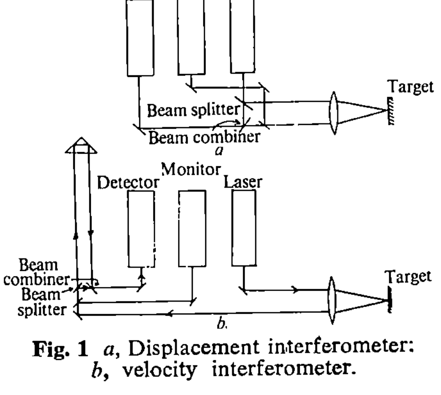

Fig. 1 *a*, Displacement interferometer: *b*, velocity interferometer.

The Systems, Science and Software SLVI-204 (S^3-204 for short) can be operated in either displacement or velocity mode and is designed specifically for the measurement of surface velocities from shock experiments. This review is not the place to discuss shock phenomena, which are well described in the literature (for example, McQueen, R. G., Marsh, S. P., Taylor, J. W., Fritz, J. N., and Carter W. J., in *High Velocity Impact Phenomena,* edited by Kinslow, R., p. 294, Academic Press, 1970). Suffice it to say that surface velocity is closely related to the internal particle velocity and gives valuable information on the behaviour of the material. The S^3-204 in the velocity mode measures surface velocity up to 3 mm μs^{-1} for a minimum time of 100 μs and with a time resolution down to 2.5 ns, covering most of the requirements for shock experiments in dense materials induced by flyer plates, explosives, pulsed electric currents and pulsed electron beams.

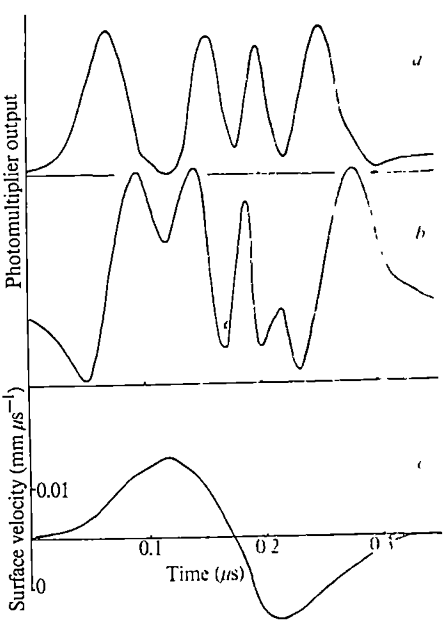

Fig. 2 Interferometer records. *a*, Photomultiplier signal (normal interference) ; *b*, photomultiplier signal with phase shift of $\lambda/4$; *c*, deduced surface velocity.

The Spectra-Physics 1 mW HeNe laser supplied with the interferometer oscillates in the TEM_{00} mode, is polarized, and produces only one axial mode. The laser is stable enough 30 min after switching it on for someone with a little practice to produce a single fringe over the whole laser spot. The laser power is adequate for polished targets, but a higher power would be necessary for poor, scratched or diffuse reflectors. The piezoelectric pulser supplied with the instrument is a considerable help in setting up and the dual pulsed photomultiplier assembly, although linear up to a few V only, operates reliably and consistently.

These are some areas of difficulty not specific to the S^3 interferometer but inherent in the use of laser interferometers in general. First, the shocked target may tilt, moving the reflected beam away from the photomultiplier. The S^3-204 can accommodate a lateral shift of 5.0 mm in the return laser beam, which with a 500 mm objective lens, corresponds to about 0.5 degree in target tilt. Objectives of shorter focal length can be used, but care should be taken in their selection, for the choice of lens is a compromise between tilt tolerance, recording time and surface velocity. S^3 offers a design service for objective lenses.

Second, electrical interference on the recorded signal increases the error in the velocity inferred. It is difficult to be precise as electrical interference is highly variable from one location to another, but for most locations the S^3-204 is probably adequately screened. If, however, as was our experience, the interferometer had to be operated outside a conventional screened room near equipment generating severe electrical interference (>1 kV m^{-1}) then the screening of the photomultiplier assembly is not adequate and local electrical double screening is necessary to reduce the interference to an acceptable level of less than 10% of the recorded signal.

Third, the interferometer does not measure the direction of the target movement, and it is in many cases not obvious from the record itself where acceleration reversals have taken place. Nonetheless, the S^3-204 can be adapted to use an optical technique of phase shifting the laser light recorded in one photomultiplier by $\lambda/4$ to obtain records in both photomultipliers that unambiguously identify acceleration reversals (Bouricious and Clifford, *Rev. Sci. Inst.*, **41**, 1800; 1970). Fig. 2 shows interferometer records obtained with this technique together with the inferred velocity. In only one record are the acceleration reversals unambiguous. The technique is available from S^3.

The S^3-204 interferometer measures reliably surface velocities from shock physics experiments, and, once a prospective purchaser has decided which of the many available options are useful to him, the instrument will provide a useful addition to any laboratory working in shock physics.

P. H. White
R. H. Gobbett

CORRESPONDENCE

Creation or Evolution

Sir,—The discussion by advocates of creation *vs* evolution (*Nature*, **240**, 365; 1972) was triggered by the "school textbook controversy" in California. Solan, at least by implication, identifies the dispute with the State of California, but a bill requiring Michigan's public schools to teach the biblical account of creation along with evolutionary theory was unanimously approved by the House Education Committee in Michigan on December 5.

The textbook controversy has both religious and scientific components. The religious arguments used by the California State Board of Education and its creationist supporters were opposed by eminent clergymen, representing several of the leading faiths, in the hearings at Sacramento on November 9. Other objections raised by the "creationists" were directed against the scientific content of evolution. These objections are uninformed, illogical, trivial, and, if they find their way into the textbooks, they will degrade the teaching of science to the children of California.

Dr John Ford, the vice-president of the Board, favours "as the best current explanation for variation among plants and other living things the Special Theory of Evolution as defined by G. A. Kerkut and others". He also states that science "classically ignores" the areas of "value systems, morals, art and poetry". Evidently, he does not know, or ignores, the contributions made to human welfare by great scientists who were also great humanitarians.

An engineer named Vernon Grose has been the Board's leading adviser on evolution. The Board elevated him to the State Textbook Commission. He is also a member of the Governor's Commission on Law Enforcement. Mr Grose's statements have made it evident that he does not have even a rudimentary knowledge of biology. He says that Pasteur's demonstration that bacteria do not arise spontaneously disproves theories of the origin of life. Mr Grose strongly opposes the concept of adaptation as an evolutionary force. He asserts that "the regular absence of transitional forms may best be explained by a creation theory", and he dislikes the concept that plants and animals have a common ancestral origin. However, he has not so far proposed a revision of the primary sequence of cytochrome *c*.

The controversy continues, and the Board, on December 14, evidently favoured introducing the teaching of creation into science textbooks. There will be more news in January, following action by a new committee of the Board that includes Dr Ford and two scientists (Richard Bube and Robert Fischer) who are active in the religiously-oriented American Scientific Affiliation.

Yours faithfully,
Thomas H. Jukes

University of California,
Berkeley, California 94720

Sir,—It is welcome that you are initiating a review of any time-honoured scientific tenet of faith—for this is what evolution has become to many of us—rather like a theological doctrine, to be defended with some passion. It is a good thing for people to question broad philosophical assumptions and keep open minds. On the issue of evolution as a primary directive force in the cosmos, I propose to do just that whilst feeling free to use the evolutionary hypothesis in relevant cases in my research and thinking.

I feel undogmatic and somewhat sceptical in the debate. Special creation cannot be proved, and a thoroughgoing evolutionary origin on the basis of environmental adaptation explains much, but leaves plenty of unanswerable queries.

My atheist undergraduate diet of Haldane, Huxley, Bernal, Wells and so on failed to satisfy me that evolution is the sole creative force behind the cosmos and the biosphere and modern *Homo sapiens*. On more recent review, I find it too much for my credulity, for reasons similar to those cited by Vanderkooi and Van Kley (*Nature*, **240**, 365; 1972). On the other hand, I find God real and His activity demonstrable over the years.

One demonstrates biogenetic evolution in the laboratory and field at species and generic level, but I doubt the validity of extrapolating these data and turning them into a first cause. Wouldn't we beat our students about the head for far less a sin?

So one opts for some creative power—I call Him God—as a first cause, which I maintain is common sense and fair science. Why did it happen—that is a non-scientific issue. How it happened is a valid question, but too difficult, except as the answer comes clear here and there from observation and experiments.

Yours faithfully,
David Allbrook

Department of Anatomy,
The University of Western Australia

Sir,—I thank you for publishing my letter on the subject of creation or evolution.

The whole fable of evolution is nothing more than a confidence trick on the part of the Devil, who is as perfectly well able to blind the eyes of men of science as he is those of lesser mortals. A theory which results in a grovellingly debased view of human origins—the absolute opposite of the truth that man was created in God's own image—and which helps to spawn such grotesquely distorted pieces of literature as Marx's *Das Kapital* and Hitler's *Mein Kampf*, can only have originated from such a source.

Yours faithfully,
ALAN RADCLIFFE-SMITH

13 Argyle Avenue,
Hounslow,
Middlesex

β-Carotene

SIR,—The following comments may be of some interest with respect to the letter of Drs Johnson and Fusaro.

While it is true that Kesten (not Keston) was the first to describe the use of β-carotene cream as a photoprotective agent, Mathews-Roth and associates were the first to show unambiguously in a number of patients and animals the effectiveness of internally administered β-carotene[1]. It should be recognized that there is a marked difference between topically and internally administered β-carotene. As Kesten showed in a single patient, topically applied β-carotene provides some protection against photosensitivity. This protection is due to the absorption of part of the incident visible light by the carotene, and hence topically applied black treacle would probably have a similar effect. When β-carotene is taken internally, its protective effect is enhanced and it seems likely that the carotene is acting not merely as a light shield but as an *in vivo* quencher of singlet oxygen. Although Kesten did administer β-carotene orally to one photosensitive patient, she did not report any definite conclusions regarding the effectiveness of the treatment.

Yours faithfully,
ANTONY F. MCDONAGH

School of Medicine,
Department of Medicine,
University of California,
San Francisco

[1] Mathews-Roth, M. M., Pathak, M. A., Fitzpatrick, T. B., Harber, L. C., and Kass, E. H., *Trans. Assoc. Amer. Phys.*, **83**, 176 (1970).

Congress *Caveat*

SIR,—We would like to reply to the letter (*Nature*, **240**, 428; 1972) about the prices of some of the excursions arranged for participants in the ninth International Congress of Biochemistry. When preparing for the Congress, the organizing committee asked a well-known Swedish travel agency, RESO, to arrange a number of visits and excursions in connexion with the Congress. The tours were to be arranged at RESO's financial risk and on the condition that they could not be cancelled on the basis of a low number of participants. The negotiations with RESO resulted in plans for those visits and excursions that are described in circular 2 of the Congress. The arrangement of these tours constitutes no source of income for the Congress but should be considered only as a service to the Congress members. The tours specially arranged for participants of the Congress provide good opportunities for informal discussions and exchange of ideas, in combination with a comfortable way of doing some sightseeing. There is no doubt that the sightseeing by itself can, in many cases, be done at a cheaper price and there are, of course ample possibilities for every visitor to arrange his own sightseeing. However, when it comes to regular sightseeing tours comparable with the Congress tours in routes, transport facilities, meals and refreshments, guide services and so on, the prices are comparable to or higher than those offered by RESO for the Congress tours.

In response to our specific question regarding the price (75 Sw. kr) of the Congress excursion through the Stockholm archipelago, we have received the following information from RESO:

The participants will sail from Stockholm to Sandhamn and back to Stavsnäs by a rented ship. In order to save time, the trip from Stavsnäs back to Stockholm will be made by rented buses. The regular voyages from Stockholm to Sandhamn and back (entirely by ship, return price 24 Sw. kr) are subsidized by the City of Stockholm, not so the Congress tour. The latter, moreover, includes a first class lunch at Sandhamn, music and coffee on board, and the services of guides. RESO will be glad to answer further questions regarding this and other Congress tours.

It is our sincere hope that all participants of the Congress will find their stay in Stockholm pleasant and profitable, and we shall do our utmost to this end.

Yours faithfully,
LARS ERNSTER

9th International Congress of Biochemistry,
c/o Svenska Kemistsamfundet,
Wenner-Gren Center, 6 tr.,
S-113 46 Stockholm

Pulsar Disclaimer

SIR, — The statement made by the authors at the end of "Periodicities in Seismic Response caused by Pulsar CP1133" by Dror Sadeh and Meir Meidav (*Nature*, **240**, 136; 1972), reading "We thank Professor C. L. Pekeris and the Applied Mathematics Department at the Weizmann Institute . . ." should not be construed as implying that I, or the Department of Applied Mathematics of the Weizmann Institute, are in any way responsible for the views expressed by the authors in this paper.

Yours faithfully,
C. L. PEKERIS

Department of Applied Mathematics,
The Weizmann Institute of Science,
Rehovot

Cancer Chemotherapy

SIR,—I wish to present a strategy for cancer chemotherapy which, to my knowledge, has not been explicitly stated in print before.

Consider two classes of substances: class A substances kill only dividing cells, class B substances reversibly inhibit the division of normal cells but do not inhibit the division of malignant cells. The strategy is to first apply a class B substance; when it has taken effect, a class A substance is applied. Both are removed before unacceptable damage is done.

The key advantageous feature of this strategy lies in the protective effect of the class B substances. This will allow larger doses of more potent class A substances to be used more frequently and for longer periods.

Class A substances are well known among current chemotherapeutic agents. Do class B substances exist?

Yours faithfully,
DAVID ZIPSER

Cold Spring Harbor Laboratory,
Cold Spring Harbor, New York 11724

Announcements

Miscellaneous

THE **Soviet State Prizes** for science for 1972 were awarded as follows:

1. To **Academician Boris Ivanovich Stepanov**, Director of the Institute of Physics of the Byelorussian Academy of Sciences, **Anatolii Nikolaevich Rubinov** and **Vasilii Andreevich Mostovnikov** for work carried out in the Institute on the optical generation of complex organic compounds in solutions and the development of a new type of laser in connexion with this work.

2. To **Dr Anatolii Filippovich Tulinov, Yurii Vladimirovich Melikov, Vatslovas Stanislavovich Kulikauskas, Grigorii Arkad'evich Iferov** and **Grigorii Pavlovich Pokhil** of Moscow State University, **Arii Aleksandrovich Puzanov** of the Ural Polytechnic Institute, **Bela Gabdulgalievna Akhmetova** of the Kazakh State University, and **Sarkis Arshavirovich Karamyan** of the Joint Institute of Nuclear Research for their discovery and investigation of the shadow effect in nuclear reactions on monocrystals.

3. To **Academician Evgenii Alekseevich Barbashin** of the Byelorussian Academy of Sciences for his work on the stability of automatic control systems.

4. To **Academician Ivan Pavlovich Alimarin, Academician Yurii Aleksandrovich Zolotov, Dr Mikhail Sergeevich Chupakhin, Yurii Vsevolodovich Yakovlev** of the Institute of Geochemistry and Analytic Chemistry of the Soviet Academy of Sciences, **Valentina Gavrilovna Goryushina** and **Dr Vsevolod Vasil'evich Nedler** of the State Research Institute of the Rare Metals Industry and **Dr Evgenii Aleksandrovich Bozhevol'nyi** of the All-Union Research Institute of Chemical Reagents and Ultra-Pure Chemical Substances, for their work on the theory and new physicochemical methods of analysis of high-purity metals, semiconductors and chemical reagents.

5. To **Dr Nikolai Mikhailovich Chirkov** for his work on the kinetics of the polymerization and copolymerization of the α-olefines.

6. To **Dr Petr Petrovich Timofeev** of the Geological Institute of the Soviet Academy of Sciences for his work on the Jurassic deposits of Southern Siberia.

7. To **Nikolai Aleksandrovich Krasil'nikov** of the Institute of Microbiology of the Soviet Academy of Sciences for his work on the biology of the actinomycetes.

8. To **Academician Nikolai Iosifovich Konrad** and his team for their work in producing the "Large Japanese–Russian Dictionary".

9. To **Dr Aleksei Andreevich Roda** of the "V. V. Dokuvaev Soil Institute" for his work on soil humidity.

10. To **Dr Vladimir Viktorovich Solodovnikov, Evgenii Pavlovich Popov,** and **Dr Viktor Vladimirovich Semenov** of the Moscow "N. E. Bauman" Higher Technical College, **Aleksandr Mikhailovich Letov, Dr Georgii Mikhailovich Ulyanov** and **Academician Boris Nikolaevich Petrov** of the Institute of Control Problems, **Germogen Sergeevich Pospelov** of the Computer Centre of the Soviet Academy of Sciences, **Dr Vil'yam Viktorovich Kazakevich** of the Moscow Polygraphic Institute, **Dr Lev Timofeevich Kuzin** of the Moscow Institute of Engineering Physics, **Dr Vyacheslav Vyacheslavovich Petrov** of the Moscow Aviation Institute, **Dr Yurii Ivanovich Topcheev** and **Dr Aleksandr Stepanovich Shatalov** of the Dzherzhinskii Institute of Military Engineering for their series of monographs on cybernetics.

11. To **Dr Vladimir Tikhonovich Renne** for his work on the theory, calculation and construction of electrical condensors.

Errata

In the article "Bacterial Reduction of Arsenate in Sea Water", by David L. Johnson (*Nature*, **240**, 44; 1972), the following corrections should be made: paragraph 1, line 5, should read "... suggest that the concentration ratio is . . . "; paragraph 2, line 6, superscripts 7–9 should be deleted; paragraph 3, line 3, 4.1% sucrose should read 0.1%; paragraph 3, line 9, the word sterile should be deleted.

In the article "New Periodic Close Packings of Identical Spheres", by J. A. R. Coutanceau Clarke (*Nature*, **240**, 408; 1972), the following corrections should be made: line 4 of the last paragraph should read " . . . results from changing (11)s"; Table 1, column 4, items 1 and 2 should each read $\bar{4}3m$; Table 2, column 7, item 15 should read $8(\sqrt{2}+\sqrt{3})$; Table 2, column $10A$, item 10 should read $(11)\times\sqrt{3}/2$.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Scottish Marine Biological Association. Annual Report for the year ending 31st March, 1972. Pp. 71. (Oban: Scottish Marine Biological Association, Dunstaffnage Marine Research Laboratory, 1972.) [2610

National Radiological Protection Board. Radiological Protection Bulletin, 1972, No. 1. Pp. 26. (Belmont, Sutton, Surrey: National Radiological Protection Board, 1972.) [2710

Department of the Environment. Bibliography: Current Information on Maintenance. Part B: Design and Maintenance. Compiled by the Property Services Agency, Library Service. Pp. 36. (London: Property Services Agency Library, Lambeth Bridge House, 1972.) 50p. [2710

Other Countries

Australia: Commonwealth Scientific and Industrial Research Organization. Division of Fisheries and Oceanography Technical Paper No. 33: Nutrient Enrichment of East Australian Coastal Waters. By D. J. Rochford. Pp. 17. (Melbourne: CSIRO, 1972.) [2310

US Department of the Interior: Geological Survey. Professional Paper 495–E: Frontier, Cody, and Mesaverde Formations in the Wind River and Southern Bighorn Basins, Wyoming. By William R. Keefer. Pp. iii+23. Water-Supply Paper 1985: Ground-Water Resources of Orange and Ulster Counties, New York. By Michael H. Frimpter. Pp. v+80+4 plates. (Washington, DC: Government Printing Office, 1972.) [2410

Smithsonian Contributions to Zoology. No. 97: The Systematics and Areal Distribution of Pelagic Cephalopods from the Seas off Southern California. By Richard Edward Young. Pp. iii+159 (38 plates). $2. No. 124: A Review of the Family Synopiidae (=Tironidae), Mainly Distributed in the Deep Sea (Crustacea: Amphipoda). By J. Laurens Barnard. Pp. iv+94. $1.25. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [2410

World Health Organization. Protection Against Ionizing Radiations: A Survey of Current World Legislation. Pp. 328. (Geneva: WHO; London: HMSO, 1972.) 28 Sw. francs; £2.80; $7. [2410

Nederlandse Vereniging voor Weer- en Sterrenkunde. Observations of Variable Stars, January–June 1972. (Report No. 22.) Pp. 5. (Groningen: Kapteyn Astronomical Laboratory, 1972.) [2410

The Museums of Man and Science/Die Museums van die Mens en Wetenskap. Pp. 16. (Johannesburg: Museums of Man and Science, 1972.) [2510

Annals of the South African Museum. Vol. 59, Part 10: A Review of the Sepiidae (Cephalopoda) of Southern Africa. By Martina A. Roeleveld. Pp. 193–313+plates 35–45. R.10.80. Vol. 59, Part 11: Discard the Names Theriodontia and Anomodontia: a New Classification of the Therapsida. By L. D. Boonstra. Pp. 315–338. R.2.10. (Cape Town: South African Museum, 1972.) [2510

New Zealand: Department of Health. Environmental Radioactivity Annual Report for 1971. Compiled by L. P. Gregory. (NRL-F/48.) Pp. 45. (Christchurch: National Radiation Laboratory, P.O. Box 25-099, 1972.) [2510

Australian Academy of Science. Year Book, June 1972. Pp. 128. (Canberra, ACTL, Australian Academy of Science, P.O. Box 216, 1972.) [2610

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Transatlantic Pressure on Research

BOTH in Britain and the United States, there is a nasty prospect that basic research will be squeezed to an unhealthy degree in the months ahead. The rumours (see *Nature*, **241**, 82 ; 1973) that the United States Administration is in a mood for yet another halt in the growth of basic science have been strengthened by the report this week (see page 158) that President Nixon intends to carry through the substance of the Ash Commission's proposals for reorganization, if necessary without consulting Congress. The fear, of course, is that the new system will make basic science dependent on the funds which several agencies think they can spare from their day to day commitments. The cancellation by NASA last week of the high-energy astronomy satellite is a sign of how easily the mission agencies can change their minds. Certainly there is no immediate prospect that the National Science Foundation will become, as it should, the chief source of funds for basic science within the federal system. For even if Senator Edward Kennedy is luckier than he has any reason to expect in persuading Congress that his bill, or some amended version of it, should be passed, the President in the present mood will only veto it. And it is only fair to say that the Kennedy bill is as much an attempt to turn the National Science Foundation into an instrument for doing jobs which the federal government at present ignores as for increasing the scale on which the National Science Foundation is enabled to sponsor basic research.

In Britain, the origin of the pressures on basic science is different, but the outlook is also gloomy. Far from seeking to hold public expenditure constant, Mr Edward Heath's government is looking for a greatly increased expenditure of government funds in the next few years but has resolved that most of the extra money shall be spent on social projects such as the creation of jobs for those who are unemployed and the relocation of industry in economically backward parts of the country and on better social services. The result is that expenditure on basic science will take a smaller proportion both of the Gross National Product and of the central government's expenditure than it has done in recent years. Yet the university system is still growing rapidly and the polytechnics are beginning to make demands of their own on the limited funds that are available. The consequences for the universities and for all institutions of higher education will be serious (see *Nature*, **240**, 515 ; 1972). The prospects for a continuing expansion of fundamental research are more gloomy still. The question to be answered, on both sides of the Atlantic, is how existing institutions should best respond to the impending changes.

One common and urgent need is that the British and the American governments should be made to recognize the potentially important consequences of the policies on which they have embarked. In both countries, there is no obvious instrument by means of which this might be accomplished. In the old days, four of five years ago, there was at least a chance that the National Science Board, ostensibly the governing body of the National Science Foundation, would emerge as a powerful source of constructive criticism. Events, however, have been a disappointment. It is entirely understandable that a committee whose chief function is to guide in an advisory capacity the officials of the National Science Foundation and, where appropriate, to lobby on the foundation's behalf elsewhere within the government, should be inhibited from having its say in public. For the same reasons, the President's Science Advisory Committee (even if it continues to exist) is bound to argue to itself that discretion is the best defence. Exactly the same considerations have prevented the Council for Scientific Policy in Britain from being an outspoken advocate of the cause of basic science. The Advisory Board for the Research Councils which has now replaced it will be even more discreet, with its membership in which government departments and the research councils will be represented as of right.

Who then is to speak for basic science? In the United States, the National Academy of Science is the obvious choice. By some means that deserves to be understood much better, the academy has managed to live off government funds and to give advice to government agencies without compromising its capacity to speak out in public. Even if the academy's council suffers as much from fuddy-duddyism as some other comparable organizations, the Committee on Science and Public Policy has a healthy tradition of outspokenness, and the academy's general membership is increasingly alert. In Britain, the Royal Society, for many reasons, some of which are good, is less well equipped to do the job. Is this a role which the British Association (with its promise of support from the Royal Society in the years ahead) might profitably undertake?

What needs to be said? The danger in the present situation is that governments will allow themselves to be carried too far by the swing of the pendulum now under way. Both in Britain and the United States in the late 1950s and early 1960s, governments were persuaded that a growth of basic science would bring industrial innovation and economic prosperity, with the result that science budgets grew quite rapidly. Now their enthusiasm has turned to disappointment, and there is a tendency to take too short a view of the value of basic science. (In this sense, the arguments about the rightness or wrongness of Lord Rothschild's proposals for reorganizing the relationship between the research councils and government departments is irrelevant, for the issue which he raised concerns the management of applied research.) The first thing to be said is that basic research is an essential ingredient of higher education, not merely because it keeps the best teachers on their toes but also because it provides them with something to teach. Who would suggest that the next generation of PhD students should be trained on problems which are either trivial or already understood? The second simple truth which governments must appreciate is that basic research is indeed a powerful source of innovation even if it is sometimes hard to quantify the economic benefits. Even recondite speculations such as the mechanism of pulsating stars (see page 161) are of considerable value to society; if the outcome is a better understanding of the difference between pulsating stars and other kinds of stars, people of all kinds, not merely astrophysicists, will find the Universe a more comfortable place in which to live. But it would be a rash man who would say that a better understanding of how stars function may not in the long run be of economic benefit. The practical problem, therefore, is the present lack of criteria, agreed between governments and the scientific community, about the scale on which basic research should be carried out. Before anything much is said, there is a need for a careful investigation of the place of basic science in modern life and then for a moderate but forceful statement of the need.

Other institutions within the scientific community can do a lot to help. Within the university system, but especially in Britain, it is important that scientists should recognize the need for selectivity and concentration. No great harm would come about if it were openly acknowledged that only some university departments in particular fields of science were important centres for research (which does not of course imply that academics in other departments need or should opt out of scholarship). In Britain, this is especially important now that the polytechnics are bent on following universities along the path of uniformly distributed research funds. The grant-giving committees of the National Science Foundation and the National Institutes of Health in the United States, and of the research councils in Britain, have a similarly important part to play in implementing such a policy. And for as long as the budgetary pressure on research funds remains as powerful as it is, the temptation to secure a lien on government funds by the setting up of research institutes separate from universities should be resisted. Especially because policies like these will require that individual researchers should frequently be prepared to forgo personal advantage for the common good, it is of the utmost importance that the steps to be taken to meet the pressures on research should be publicly discussed and widely agreed.

Dr Medvedev in London

THE Soviet government has done well to allow Dr Zhores Medvedev to spend the coming year at the National Institute for Medical Research at Mill Hill, London. For several years Dr Medvedev has been campaigning for more liberal arrangements for Soviet scientists to communicate with colleagues elsewhere, and has suffered much inconvenience as a result. Perhaps the Soviet government has wryly calculated that it will be best for both of them if Dr Medvedev now spends a year rusticating in Britain and there is always of course the chance that he may find the traffic is not an unmitigated blessing, that even Western scientists are sometimes over-reticent and that the common concern about research budgets can depress the spirit. Yet the Soviet government should know that giving a passport and an exit visa to Dr Medvedev and his family will go a long way to ease relations with the scientific community in the West. For Dr Medvedev has been something of a test case, and in the past few months there has been much muttering about the wisdom of participating in international conferences organized in the Soviet Union. This should now be in large measure dissipated (which is not to say that Western scientists would not welcome much less formal means of spending time with individual Russian scientists and of communicating with them). And it goes without saying, of course, that if the Soviet government's liberal action in the past few days should be followed by a revocation of his exit visa, unthinkable though that may be at present, there will be a howl of protest and lasting damage to cultural relations with the Soviet Union will be done.

By his own account, Dr Medvedev is a Russian patriot and is determined to return to the Soviet Union when his year is up. It is therefore important that he should be helped as much as possible to devote himself singlemindedly to his research, and that he should not be drawn into situations which could be interpreted as disloyal to the Soviet Union. For, however much people in the West may think it their right to go abroad and criticize their governments, it is well known that the Soviet government takes a different view.

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100 Years Ago

THE NAVY AND SCIENCE

IT would be difficult to estimate the many excellent effects that are likely to result from the establishment of the Royal Naval College, which, as has been at last authoritatively intimated, is to be opened on February 1, in those noble halls at Greenwich that for so long have been associated in another way with the British Navy. Her Majesty's Government deserve the highest praise for the wisdom—provokingly tardy though it has been—displayed in the thorough and handsome provision they have made for the scientific education of our naval officers. Much that is sarcastic, no doubt, might be said on this tardiness of a Government which seldom moves until it is driven; but as we fear this would do little good, we shall only express a hope that in future when they are compelled to take action in any matter, especially if it be scientific, they will do so as decidedly and sweepingly as they have done in the present instance.

Movements of the Earth's Surface

IT is, I believe, commonly supposed by geologists that the movements of the surface of the earth are caused by the refrigeration and contraction of the interior. But since the glacial epoch the surface of the earth has become warmer; consequently since that time a heat wave must have been passing from the surface towards the centre; and consequently since that time no refrigeration nor contraction of the interior can have taken place. If, therefore, movements of the earth's surface were due to this cause only, no such movements should have taken place since the glacial epoch. F. W. HUTTON

Wellington, New Zealand, Nov. 10, 1872

From Nature, 7, 217, *January* 23, 1873.

OLD WORLD

University Interest Aroused

SEVERAL university departments have submitted applications to the Science Research Council for grants to work on superconducting a.c. generators following a report by an SRC working party on the subject last November (see *Nature*, **240**, 175 ; 1972). Among these are the Universities of Oxford, Southampton and Leeds ; other requests for support are on the way.

The Oxford application is from the mechanical engineering department to work on the cryogenic aspect of a.c. generation, Southampton's interest comes from both the mechanical and electrical departments, and the Leeds application is also from the engineering department.

Those applications that reached the SRC's Electrical and Systems Engineering Committee by the last closing date for applications (December 15, 1972) will be considered by the committee in March after the working party, which is to be reconvened, has offered its opinion on them in February, and after the council, in the same month, has decided its attitude to the working party's report and how much money to make available.

Other applications which reach the SRC by its next closing date for applications, the beginning of April, will be considered in that month, and the committee hopes to see at least three or four groups working on the lines recommended in the report by the end of 1973, although a spokesman for the SRC was unwilling to discuss individual applications last week.

When the committee circulated the report, it asked for comments on it and for suggestions of other fields to which superconductivity could be applied. Reaction so far has been largely favourable. Most consider that the report is a reasoned assessment of the situation, although some feel that the case for initiating research on superconducting generators has not been proven. Nobody, it appears, is of the opinion that the working party was too timorous in its suggestion that research should start quickly, but on a comparatively small scale.

The request for suggestions of other areas to which superconductivity could be applied has been disappointing. One or two ideas have been put forward, but with the exception of a.c. generation and d.c. motors, superconductivity at present appears not to be as useful a phenomenon as it seems to be at first glance.

The Electrical and Systems Engineering Committee is also examining other areas of its brief in an effort to redefine the direction of its work. A report on electrical machines other than superconductors is due shortly, and the committee is also to examine work on solid state devices and telecommunications.

But superconductivity looms largest on the committee's agenda at present, as it does at International Research and Development in Newcastle where £1.5 million has been spent on research into a.c. and d.c. superconducting machines in the past ten years.

IRD, under the enthusiastic guidance of Mr A. D. Appleton, its head of electrical engineering, has undertaken much of the industrial superconducting work in Britain. Its greatest success has been with d.c. machines, but since 1968 a.c. generation has also played a large part in its work. The company will be closely involved in the planning and coordination of the research on a.c. generation that the SRC is to finance, for one of the strongest stipulations of the working party's report is that research must be closely linked to industry.

IRD has examined generator designs up to 2,000 MW, and is already talking to many of the academics interested in undertaking work in the field. IRD—as was made plain by the SRC working party on which Mr Appleton represented the company—is eager to build a 60 MW generator, at a cost of about £2 million. Such a machine would be by far the largest superconducting generator ever built, the only competition being the Westinghouse 5 MW machine. Mr Appleton points out that a 60 MW machine is big enough to give a real idea of the problems involved (unlike a 5 MW machine) as well as having the advantage that it can be installed in a power station to replace one of the 60 MW sets that the Central Electricity Generating Board is currently phasing out, thus providing genuine working conditions and removing the not inconsiderable problem

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OPEN UNIVERSITY

First Degrees Awarded

THE Open University announced the award of its first degrees last week. Eight hundred and sixty-seven students have qualified for the university's BA degree and can now go on to acquire an honours degree after a further one or two years.

The Open University is at pains to point out that the 867 are atypical students. All have passed their degree in just two years, acquiring the six credits necessary by being given two or three credit exemptions (for previous academic qualifications) and by obtaining two further credits each year—the maximum. Next year's graduates should be much more typical.

The university has remarkably few statistics available about its graduates. These are all in the computer at present is the claim, so that it is not even known whether the new graduates are predominantly science-based or arts-based.

Seven out of ten of the university's other students gained credits in the 1972 examinations. A total of 36,076 foundation and second level examinations were taken by 25,203 students ; 23,578 passed one or more course examinations, thereby gaining a credit, and 33,458 credits were awarded in all. The overall course pass rate for the year was 71.4 per cent for foundation level courses and 70.5 per cent for second level.

While it is not yet possible to calculate how many students have dropped out of the Open University since it started—students can accumulate the credits needed for their degrees over several years—the dropout rate on courses is less than 25 per cent. Seventy-eight per cent of students who started courses took the examinations, and of those who took them, 91.7 per cent passed.

The Open University is well pleased with the results which are published just as it launches the largest part of this year's advertising campaign to encourage applications. About £20,000 of the £35,000 advertising budget is to be spent in the next few weeks on advertisements in regional and national newspapers and on the university's first venture into television commercials. Advertisements will be run on Border Television starting this week and their effect assessed as a pilot scheme for a fuller use of television. Although advertisements will appear in more than fifty national and local papers, the university is concentrating its efforts on those parts of Britain which have had a poorer application rate so far—the north, Wales, the west midlands and the north-west.

of finding a suitable test load. The snag at the moment is finding £2 million.

On d.c. motors, however, IRD has progressed much further. The biggest remaining problem, according to Mr Appleton, "is persuading people to accept a new technology". IRD's 3,250 brake horse power motor successfully drove a water pump at Fawley power station for four months in 1971, although problems with the refrigeration unit hampered work. IRD's current project involves building a 1 MW propulsion unit for the Ministry of Defence which will undergo trials at IRD shortly and will be put into a naval ship later this year. The British Steel Corporation is also interested in using a superconducting motor to power its steel mills, and if that becomes a reality, and is successful, the day may not be so far away when superconducting d.c. motors become a standard part of industry's equipment.

RESEARCH AND DEVELOPMENT

Ways and Means

PROFESSOR H. B. G. CASIMIR, president of the European Physical Society and until recently head of research at Philips, Eindhoven, publicized his reservations about the customer-contractor principle as applied to scientific research in a lecture given at the Institution of Electrical Engineers last week. He proclaimed that "scientific originality cannot easily come from a sense of duty" and went on to say that in his experience the best scientific work is usually done by a person straying a little from his usual discipline to involve himself in a subject that fascinates him. The inconvenience that this may cause, Professor Casimir said, is the price that must be paid for a first-class mind.

Speaking of the relationships between technology and basic science, Professor Casimir drew attention to the way in which the dependence of one on

EDUCATION

University Physics

THE Nuffield Foundation has allocated £55,000 to bridge the gap between A-level and first-year university physics. The grant made on January 1 is for five years and is allocated on the basis of a successful pilot study carried out in 1971 and 72 at the physics departments of the universities of Birmingham, Keele, Surrey, York, Chelsea College at the University of London and University College, Cardiff.

Mr R. A. Sutton of the physics department at Cardiff, the only full-time person working on the project at present, said this week that there was an increasing problem of matching the wide range of backgrounds and ability of sixth formers to the needs of university first-year physics courses. A-level physics syllabuses vary from examination board to examination board and it is common for students to omit some parts of the syllabus when studying for their examinations. Such gaps in knowledge only become important when further work is being built on the missing parts in university. But, according to Mr Sutton, a much more important factor is the differing emphasis laid on the syllabus by school teachers.

With the problem areas now identified, during the next five years the project will be directed towards developing self-teaching units of various kinds to help students over the transition period between school and university. Efforts will also be made to refine the diagnostic procedures and the effectiveness of the self-teaching units will be analysed as the project proceeds.

The self-help material is in no way, said Mr Sutton, to be construed as replacing the A-level syllabus, and it is hoped that one of the side benefits of the project will be that university teachers will devote some time to thinking about how physics is taught. Some of the grant may also be spent in appointing temporary lecturers so that the regular staff can spend their undivided attention in preparing self-teaching manuals, or to appoint people to help the regular physics department staff to prepare the aids.

The project is guided by a committee consisting of Professor C. A. Taylor of Cardiff, Professor E. J. Burge of Chelsea College, Professor S. J. Eggleston of Keele, Professor O. S. Heavens of York and Professor K. W. Keohane of Chelsea College. It is not the first attempt to try and correlate a subject in school and university—the Nuffield Foundation has supported a similar project in biology since 1969.

CHESS

Hartston Misses Narrowly

THERE is a long tradition going back to 1895 of International Chess Tournaments held in the town of Hastings, but in some ways the ending of the most recent tournament which was held during the past three weeks has proved to be one of the most interesting of all.

The tournament was won by Bent Larsen of Denmark, who is certainly one of the most successful tournament players of recent times. Larsen played with the utmost aggression and self-assurance and scored 11½ points from his 15 games. Occasionally his style allows for some drastic defeats, and he was decisively beaten at Hastings this year both by Uhlmann of East Germany and by Radulov of Bulgaria. These defeats, however, did not deter Larsen from winning no fewer than 10 of his remaining games, including wins from each of his last four games in the tournament, a time when lesser players begin to tire and look for comparatively restful draws.

The East German, Uhlmann, ran Larsen a close second with 11 points, and when on form (as he was at Hastings) is clearly a formidable player with a similar fighting spirit to Larsen.

One surprise of the tournament was the performance of the Englishman, William Hartston, who came a clear third. Hartston, at 25, has only just qualified for his International Master title and at Hastings only narrowly missed obtaining the first leg of a "grand master" qualification. The measure of his performance can be gauged by the fact that he finished above six recognized international grand masters (including one ex-world champion), and that as late as the thirteenth round had been joint leader of the tournament. His last two games, however, resulted in losses to the eventual first two prizewinners, Larsen and Uhlmann, but his score of 9½ points was still an excellent one.

Perhaps the greatest surprise of the tournament, however, was the relatively poor showing by the Russian representatives, Tukmakov and Smyslov, who finished only in equal fifth and ninth places respectively. At last year's Hastings Tournament, the two Russian players, Korchnoy and Karpov, finished in equal first place, but since the strafing of the top Russian players by Fischer in recent times a slightly unsettling effect has been noticed in the whole Russian camp of chess players, and their play has been rather less convincing than in previous years.

The following game is the critical and hard-fought fourteenth round game between Hartston and Uhlmann.—J.P.

Hartston (white) v Uhlmann (black)

FRENCH DEFENCE

White	Black
1 P-K4	P-K3
2 Kt-QB3	P-Q4
3 P-Q4	B-Kt5
4 P-K5	Kt-K2
5 P-QR3	BxKt ch
6 PxB	P-QB4
7 Kt-B3	B-Q2
8 P-QR4	Q-R4
9 Q-Q2	QKt-B3
10 B-K2	QR-B1
11 PxP	Kt-Kt3
12 0-0	QKtxP
13 KtxKt	KtxKt
14 Q-K3	Kt-Kt3
15 B-R3	B-B3
16 P-KB4	0-0
17 Q-R3	QR-Q1
18 B-QKt4	Q-B2
19 B-Q3	P-B4
20 Q-Kt3	R-B3
21 Q-K3	P-QR4
22 B-R3	BxP
23 B-Kt2	B-B3
24 P-B4	R-B2
25 P-KKt3	R-K2
26 QR-K1	Q-Q2
27 Q-Q4	P-R5
28 P-R4	PxP
29 QxQ	R(Q1)xQ
30 BxQBP	R-Q7
31 R-B2	RxR
32 KxR	K-B2
33 P-R5	Kt-B1
34 B-K5	R-K1
35 B-Q6	Kt-Q2
36 P-Kt4	PxP
37 P-B5	Kt-B1
38 K-Kt1	K-B3
39 B-Kt ch	KxP
40 BxP	Kt-Q2
41 B-Q3 ch	K-Kt4
42 BxP	KxP
43 R-K2	K-Kt4
44 B-Q4	B-B6
45 R-Q2	Kt-B1
46 B-Q3	Kt-Kt3
47 R-R2	P-K4
48 B-K3 ch	Kt-B5
49 R-R7	P-R6
50 B-B4	K-Kt3
51 R-R2	R-QR1
52 P-B3	B-Q4
White resigns	

another has changed. Steam engines were well established before thermodynamics as such saw the light of day, but the situation soon reversed and the properties of electrons, for example, had to be understood in some measure before any kind of electronic device could be constructed. At present, industry rarely uses the most recent advances in basic science, however, and the "lead time" is often of the order of fifteen to twenty years. On the other hand, scientists, especially astronomers, who make use, for example, of satellite systems, manage to get hold of the most recent technology. And often the lead time is almost zero.

Most scientists, Professor Casimir said, spend much of their time filling in gaps rather than making fundamental discoveries. But when they are filling gaps for the benefit of industry, they must avoid excessive control by the interested industrial concern, which must also resist the temptation to be overbearing.

Professor Casimir also described the different ways in which a company can organize its research and development. First, there is an arrangement along the lines favoured by Bell Telephone Laboratories in which a central research and development organization is responsible directly to the board of management of the company. One objection to this is that the manufacturing units within the company have too little say in the formulation of research policy. Second, each manufacturing unit within a company can make its own research arrangements. If there are n units then there are $\frac{1}{2}n\,(n-1)$ interfaces between research departments across which meaningful dialogues have to be conducted if advantage is to be taken of work done by the others. Third, there is an arrangement with n interfaces, namely one in which all units have facilities for development but where there is also a central organization for advanced research and development. This is the scheme adopted by Philips, and it has the edge, as far as problems of communication are concerned, when n is four or more, that is in a moderately diversified company.

ITINERANTS

Medvedev Arrives

ZHORES MEDVEDEV arrived in Britain this week to take up a one-year appointment at the National Institute for Medical Research at Mill Hill. He arrived by train on Sunday accompanied by his wife, who is also a biochemist, and his 16-year-old son. His eldest son is still in the Soviet Union.

Dr Medvedev said this week that he is looking forward to his year in Britain and he is hoping that some experiments can be carried out at Mill Hill to try and test his theories on the mechanism of the ageing of cells.

The visa that was issued to Dr Medvedev on December 12, 1972, is valid for one year but the family's passports are valid for two years. It is possible in principle, said Dr Medvedev this week, for the visa to be extended for a further year but it is too early yet to say whether his work will make it necessary for him to apply for an extension.

Dr Medvedev does not know whether he will visit other countries during his leave from the Soviet Union. He has had invitations to attend conferences both in Europe and in the United States but before making any arrangements he will find out from the Soviet Embassy whether his visa is valid for travel to countries other than Britain. He particularly would like to visit Berkeley, California, in August to attend the 13th International Congress on Genetics.

ASTRONOMY

Plumian Professorship

THE saga of astronomy in the University of Cambridge had another chapter added this week with the news that Professor Martin Rees is to become Plumian Professor of Astronomy and Experimental Philosophy at the University.

Professor Rees, who only took up his present position as Research Professor of Astronomy at the University of Sussex in October 1972, was previously at the then Institute of Theoretical Astronomy at Cambridge as a research fellow in Professor Sir Fred Hoyle's group.

But in the past year astronomy at Cambridge has suffered much publicity and some losses. In April 1972, Sir Fred announced that he was resigning from the Plumian Chair, and speculation at the time ascribed this to, among other factors, his disagreement with the reorganization of astronomy teaching and research at Cambridge (*Nature*, **236**, 419; 1972).

Under the new arrangements, which came into force last August, the Institute of Theoretical Astronomy and the University Observatories were merged into the Institute of Astronomy, and Professor Rees will be one of the three professors at the institute. Each professor in turn is expected to hold the directorship of the institute; the present director is Professor Donald Lynden-Bell, who himself only took up his position as Professor of Astrophysics at the university last October.

The University of Sussex will undoubtedly not be pleased to lose a professor so soon after his appointment, but nobody will begrudge Professor Rees his appointment to the premier chair of astronomy in Britain at the age of 30.

Alice in Eco-land

"I SEE" said Alice "that the *Sierra Club Bulletin* has an ad for boots made of mustang leather, and a long article asking us to protect wild horses. Why?"

"Because" said the Mad Hatter "the word 'mustang' in the ad only means that the boots are mustang colour. The leather is cowhide, so everything is ecological."

"But" said Alice "cows spend their lives giving us milk. They are very friendly. Why do we make them into boots and hamburger, if we protect mustangs?"

"Cows are not an endangered species," replied the Hatter, "they are only endangered individuals. They are not part of the web of life. So they don't matter."

"Why are mustangs an endangered species?" asked Alice. "They are just horses that have run wild. There are lots of tame horses. If a cow ran wild, would it be an endangered species?"

"No," said the Hatter. "It would be rounded up, and made into hamburger."

"If I were a cow" said Alice "I would ask a genetic engineer to make me into a mustang."—*T. Jukes, University of California, Berkeley, California.*

NEW WORLD

Science and the Executive Branch

by our Washington Correspondent

EARLY in 1971, President Nixon asked Congress to approve far-reaching plans to reorganize the federal bureaucracy along functional lines as recommended by the Ash Commission. The heart of his proposals was the amalgamation of several departments and agencies into four conglomerate departments to be called the Departments of Natural Resources, Human Resources, Community Development and Economic Affairs. But the plans died in the committee rooms of Capitol Hill and did not get past either the House or the Senate.

President Nixon has served notice, however, that he will again send essentially the same reorganization plan to Congress in the next few months. He has also put into effect some changes in the executive branch which move as close to his reorganization plan as possible without requiring congressional approval. The changes to some extent involve the planning of science and technology, and they also provide some pointers to the possible fate of the Office of Science and Technology—an issue which was still the subject of considerable speculation and uncertainty at the end of last week (see *Nature*, **241**, 82 ; 1973).

On the domestic front, President Nixon has set up three policy-making committees, each of which will be run by a cabinet member and which will in effect be committees of the Domestic Council—a committee set up in the White House in 1969 to advise the President on domestic affairs. The committees will be concerned with natural resources, human resources and community development ; they will be composed of the heads of departments and agencies whose activities fall in those categories and their function will be to plan and coordinate policies.

The chairman of each committee will become a counsellor to the President, and it takes no stretch of the imagination to see that their roles will come close to the roles prescribed for the heads of the three conglomerate domestic departments which President Nixon wants to set up.

Mr Earl Butz, Secretary of Agriculture, will take on the additional post of Counsellor for Natural Resources. Mr Caspar Weinberger, the Secretary-designate of Health, Education and Welfare, will also become Counsellor for Human Resources. Mr James Lynn, the Secretary-designate of Housing and Urban Development, will become Counsellor for Community Development.

In addition, John D. Ehrlichman, Chairman of the Domestic Council itself, will provide liaison between the new counsellors and the President, and George Shultz, the Secretary of the Treasury, was last month given the task of planning economic policies in much the same way as the head of the proposed Department of Economic Affairs.

Ehrlichman said last week that the committees will be concerned with policy issues which at present involve several different departments and agencies. In the past, he said, such issues have been dealt with by White House staff because they have been the only people able to bring together the views of officials in several departments. "This is, in effect, forcing down out of the White House to the cabinet members themselves—off the President's desk, onto the counsellors' desks—these policy development issues," he said. One result will be a 50 per cent reduction in the size of the White House staff.

If the counsellors' areas of responsibility match those of the heads of the proposed conglomerate departments—and Ehrlichman confirmed that such would be the case—Butz's committee will be concerned with such issues as energy policy, resource development and conservation. Weinberger's committee will be concerned with most of the present functions of the Department of Health, Education and Welfare, some of the functions of the Department of Agriculture such as the school lunch programme and meat and poultry inspection and some functions of the Department of Labor. And Lynn's committee will be concerned with most of the functions at present being performed by the Department of Housing and Urban Development, together with policies concerning mass transportation and highway construction.

How does science and technology fit into this new structure? The first thing to be said is that the executive reorganization plan submitted to Congress two years ago would have had little effect on most of the agencies with primary responsibility for science and technology—the National Science Foundation would scarcely be affected, for example, nor would NASA. But the plan does involve significant changes in the Atomic Energy Commission, the National Oceanic and Atmospheric Administration and the scientific activities of those departments which would be grouped together in the super-agencies.

The original idea was to move NOAA lock, stock and barrel into the Department of Natural Resources, and so presumably one of Butz's responsibilities will be to help integrate its policies with, for example, those of the Fish and Wildlife Division of the Department of Interior and the soil and water conservation services and forest services of the Department of Agriculture.

As for the Atomic Energy Commission, its civilian power, raw materials, enrichment and Plowshare programmes were scheduled to be moved into the Department of Natural Resources and so Butz will also have a finger in those pies while the chairman of the AEC, when he is appointed, will presumably get a seat on Butz's committee. One objective of that committee will clearly be to develop an energy policy for the United States.

The reorganization leaves aside the question of what would become of the AEC's physical research and weapons development divisions. Neither the plan submitted to Congress two years ago nor the charges announced last week had anything to say about those activities.

One aspect of Butz's new appointment has raised some muted comment from environmentalist groups. The chief responsibility of his committee will be to develop policies for resource utilization, and many of the issues it will consider involve environmental considerations. What, then, will be his relationship with the Council on Environmental Quality, which is charged with the task of overseeing the development of environmental policies?

President Nixon announced last week that all three members of the CEQ have been reappointed for his second term, thereby laying to rest rumours that he would dismantle the council, but whether it will be able to hold its own with Butz's high-level committee remains to be seen. In any case, the fears of the environmentalists will not be lessened by a statement made by Butz at a press conference last week that "when we run short of power, the first people to have their power shut off should be those who blocked the Alaskan pipeline".

One body which is also likely to be profoundly affected by the reorganization announced last week is the Office of Science and Technology. For one thing, the committees of the Domestic Council which have been set up are likely to concern themselves with some questions of science and technology which would normally have fallen in the purview of OST—the development of an energy policy, for example. And for another, much of the work of OST during the past two years has been concerned with the relationship between investment in research and development and general economic policies. Such questions would presumably fall into the area of responsibility of Mr Shultz and the proposed Department of Economic Affairs.

These considerations, coupled with the fact that Dr Edward David and Dr John Baldeschwieler, the Director and Deputy Director of OST respectively, both left the White House earlier this month, have increased speculation that OST will be scrapped. One possibility which is now being voiced is that some of the staff of OST will be moved over to the Office of Management and Budget, while others may serve on the staffs of the committees of the Domestic Council. No plans have been announced, however, and members of OST are anxiously awaiting news of their future.

SCIENCE POLICY

Help for Kennedy

by our Washington Correspondent

A bill was introduced into the House of Representatives last week which could greatly influence the prospects for Senator Kennedy's National Science Policy and Priorities Act. Numbered HR 32, the bill proposes essentially the same programmes and objectives as Kennedy's bill (which is numbered S 32), but attempts to overcome one of the chief objections that has been raised against Kennedy's proposals—that they would undermine the responsibility of the National Science Foundation to foster basic research.

Introduced by Representative Alphonzo Bell, a Republican member of the Subcommittee on Science, Research and Development, the bill would create two new agencies within the National Science Foundation—the Civil Science Systems Administration which Kennedy proposes and a Science, Research and Education Administration. The idea is for the Civil Science Systems Administration to sponsor applied research and development to solve urban problems, while the Science, Research and Education Administration would be concerned with the support of basic research and education. An important part of Bell's proposals is that the latter agency should receive at least 40 per cent of NSF's total budget and that no funds could be transferred between the two branches of NSF.

Bell says that he has introduced the bill to meet objections raised during hearings on Kennedy's bill conducted by the Subcommittee on Science, Research and Development last year (see *Nature*, **239**, 302; 1972). But his bill retains the proposal that spending on civilian science and technology should equal that on defence science and technology, and calls for a total expenditure of more than $1,000 million over three years. It would therefore probably be vetoed by President Nixon if it were passed.

DRUG LICENSING

FDA at Law

by our Washington Correspondent

The US Supreme Court has decided to resolve a legal conflict between the Food and Drug Administration and the several drug manufacturers who have challenged the FDA's procedures for taking ineffective drugs off the market. The future of the FDA's drug control programme could well hang on the court's decision.

The Supreme Court will review five cases which have recently been tried by lower courts and which turn on the question of whether the FDA is obliged to hold public hearings when it bans supposedly ineffective drugs. Also at issue is the scope of the provision in the food and drug laws which requires drugs to be effective and the role of the courts in deciding manufacturers' appeals against FDA actions. The Supreme Court is expected to review the cases in the spring and to hand down a decision by June.

The basis of the court cases is an amendment to the food and drug laws passed by Congress in 1962. Before then, the FDA had power to remove from the market only drugs judged to be unsafe. The 1962 amendment, however, gave the agency the power to require that drugs be effective as well as safe and the FDA set in train a review of the efficacy of the 4,000 or so drugs that it had then approved.

The review, carried out by the National Academy of Sciences, has already led the FDA to withdraw approval for more than 1,300 drugs. Such numbers would clearly be difficult, if not impossible, to handle under the agency's standard regulations for removing products from the market, which provide manufacturers with the right to a public hearing if they wish to contest the FDA's actions. The agency thus published new regulations in 1969 for dealing with supposedly ineffective drugs which, in short, give manufacturers the right to a public hearing only if they can provide substantial scientific evidence to show that their product is effective.

In one specific case, a drug called Lutrexin, the FDA ordered the manufacturer to withdraw the drug from the market because the NAS had found it to be only "possibly effective". The manufacturer asked for a public hearing, which the FDA denied, and the case then went to a court of appeals. The upshot was that the court ruled against the FDA, and the FDA subsequently appealed against the decision to the Supreme Court on the grounds that it would require the agency to hold public hearings on nearly all its cancellation orders. The FDA argues that such a requirement would cause a massive log-jam and effectively block the whole programme.

Another case being reviewed by the Supreme Court involves the question of whether the FDA has the power to ban from the market drugs which it has not specifically approved in the first place—the so-called "me too" drugs. Such drugs were allowed on the market without specific FDA approval because they have identical, or very similar, formulae to other drugs which had already been approved as safe.

The FDA claims that if it orders one drug off the market because it is ineffective, all others with the same formula should meet the same fate. A court in Philadelphia backed the FDA last year, but a court in Virginia ruled that federal courts and not the FDA must decide whether "me too" drugs could be ordered off the market under the 1962 amendment. This is another of the nuts the Supreme Court must attempt to crack.

OBESITY

Amphetamine Ban

In spite of legal challenges to its procedures for ordering ineffective drugs off the market, the Food and Drug Administration has decided to stop the sale of anti-obesity products which combine amphetamines with other drugs. The agency believes that such combinations are no more effective than amphetamines alone, and has already taken steps to prevent their manufacture by asking the Department of Justice to eliminate production quotas for the products. Last month, the FDA warned that even amphetamines alone are of only marginal value in the treatment of obesity, and several witnesses before the Senate Select Committee on Nutrition and Human Needs urged that the combination drugs should be banned (see *Nature*, **240**, 436; 1972).

The Biggest World Model So Far

from our Special Correspondent

Geneva, January

THE World Employment Programme on which the International Labour Office is likely to have spent $2 million in the four years to 1975 has had the somewhat unexpected result of having thrown up a dynamic computer model comparable in many ways to the Meadows model, developed for the Club of Rome at MIT, but which is at once much larger and more sophisticated. The model is being used to test the interactions between population growth and employment and is intended to throw light on questions of employment policy in developing countries. It is called Bachue—1 after the Colombian goddess of love and fertility and harmony between nature and man.

Some idea of how ambitious the simulation model is can be gathered from the fact that even the refined version of it occupies more than 600 K of storage space on the IBM 370 computer installed at the International Computing Centre in Geneva. The first run of the model a few weeks ago occupied no fewer than 796 K of the 1,000 K core, leaving precious little room for the operational programs necessary to allow the computer to function properly. The work at the ILO has been directed by Dr Richard Blandy, an Australian economist who has just returned to Flinders University, Adelaide. Day to day responsibility for the development of the system has been shouldered by Dr René Wéry, with Mr Ray Curnow of the Science Policy Unit, University of Sussex, acting as a consultant.

Everybody concerned with the project is full of admiration for Professor Jay Forrester's DYNAMO Language in which the programs have been written and especially for the flexibility which this permits and for what are called the "debugging facilities" which, among other things, allow the system of programs to make explicit assumptions about the values of particular parameters when these have been incompletely specified. But DYNAMO Language is extravagant in its use of storage space, so that there are plans—or hopes—to rewrite the lot in Fortran.

The simulation model differs from the Meadows model in the degree to which the variables are disaggregated. Population, for example, is represented by separate variables for each interval of five years between birth and old age, and these categories are further subdivided by sex and residence in urban or rural areas. In the version of the model now functioning, fertility (or, more specifically, the number of births each year to women of different ages and in different categories) is reckoned to be a function of child mortality (and positively correlated with it), the education of adults, the opportunities for women to work in modern jobs, the numbers of unpaid family workers in the labour force, the education of children and the average income of households. The model also makes possible a variety of assumptions about the effectiveness of family planning. One of the innovations built into Bachue—1 is the possibility of simulating the migration of workers from country to town.

Compared with previous models, the ILO simulation breaks new ground in its detailed description of the labour force, but its authors acknowledge that data from developing countries which purport, for example, to indicate the proportion of the female population in work of various types are probably highly suspect. Data to represent the several categories by which the educational system is described are probably easier to come by but the assumptions which have been made about the social and economic impact of different kinds of education are probably among the most difficult of all to test. The economic parts of the model are impressively disaggregated—with the problems of developing countries in mind, the ILO team has distinguished between modern and traditional agriculture, modern and traditional manufacturing industry and employment in service functions.

It goes without saying that the ILO model differs from the Meadows model in that it makes no allowance for such things as the effect of pollution on mortality nor of the availability of natural resources other than food. For that matter, the model also fails to allow for differences of caste or race within countries.

The immediate objective is to use the model as a means of telling which kinds of development in a developing country are most likely to help shrink the size of the labour force without work or engaged in non-productive tasks. To provide some yardstick of what will happen, the modellers have used data from countries in Latin America between 1960 and 1970 to provide a starting point for a forty year simulation. They acknowledge that a great deal of work remains to be done before the model can be regarded as mathematically self-coherent and stable to transients, and before the assumptions which have been built into them can be tested; some will no doubt be validated, others will need further refinement.

What is likely to be the value of this computer model? Although the original incentive for its development was the haunting unemployment problem in developing countries, the model is plainly able to throw light on a wide range of problems concerned with development. One possibility, for example, is that the model may throw light on the economic consequences of rural-urban migration. With the assumptions so far made, such demographic movements may have the effect, for all their immediate or at least conspicuous ill-effects, of making possible a more rapid growth of family incomes. With the assumptions so far incorporated, the model also suggests that an immediate reduction of fertility will not bring social and economic benefits within a decade or even two, although it must be acknowledged that the cost of capital investment in education and health care may not be adequately catered for in the model.

This is why one of the most attractive features of this ambitious exercise in computer simulation is that the modelling is supported by a vast programme of field studies in which attempts will be made to gather from developing countries some of the data on which refined assumptions may be formulated. Unlike some others, the ILO's model is a starting point for a programme of social and economic research which is certain to be made more pointed by the preliminary results of the simulations, but which is a sufficient objective in itself.

Those responsible for the computer modelling hope that in the months ahead it will also be possible to use the model as a means of generating hypotheses for other parts of the World Employment Programme. One of the most stimulating of these is the attempt which is being made to assess the impact of new technologies on employment in developing countries. Should a growing nation invest its capital in agriculture, in advanced technology such as nuclear power or in something half way in between? Several field studies have already been commissioned of the operation of modest industrial enterprises, canning factories for example, on the social condition of the communities in which they are placed in countries such as Kenya. In due course it may be possible to develop yardsticks by means of which developing countries may decide what kinds of new developments will be best. Then will come the task of persuading aid-giving countries that they should be backed with hard external currencies.

NEWS AND VIEWS

Problems of Understanding Pulsars

PROGRESS in pulsar theory is slower than might be expected from the wealth of observational data now available. An important step forward was the statement by Goldreich and Julian in 1969 (*Astrophys. J.*, **157**, 869) that a rotating, magnetized neutron star must be surrounded by a very remarkable co-rotating magnetosphere, in which gravity counts for almost nothing and only electrodynamic forces determine the particle motion out to a distance where the co-rotation velocity approaches the velocity of light. Mestel (*Nature Physical Science*, **233**, 149 ; 1971) has recently given a more general account of this theory. But astronomers seem to be no nearer to an understanding of the basic radiation process. If anybody claims to understand pulsars, let him answer the question "How do they pulse?"

What is needed is a twin attack from observation and from theory. A co-rotating magnetosphere provides a fairly straightforward analytical problem, provided that the particle density is so low that it does not affect the magnetic field. This is almost certainly not the case in the interesting region close to the velocity of light circle, but there are other problems extending throughout a more realistic magnetosphere. A self-consistent solution including a full complement of particles and magnetic field must face problems such as the following.

- Do the particles gain and radiate most of their energy close to the pulsar surface or near the velocity of light circle?
- What are the particle trajectories near the velocity of light circle?
- Is there a complete charge separation in clearly defined regions of the magnetosphere?
- Is the charge of the outward electron flow balanced by a return flow of electrons or by an outward flow of protons?
- What is the mechanism for bunching which leads to coherent radio emission?

Observation may provide some help in describing the geometry of the field and the electron trajectories in the emitting region. But to date there is no agreement about the location of the emitting region, and no clear interpretation of the polarization measurements which should provide a description of the magnetic field. There should be some critical experiments which could provide a real guide to the field configuration, but none has been forthcoming so far.

Another approach is to consider how the pulsar magnetosphere might evolve as the spin rate decreases. An interesting way out of the analytical problem then emerges: old pulsars might not have a dense magnetosphere at all. Ruderman (*Phys. Rev. Lett.*, **27**, 1306 ; 1971) has suggested that slow rotation provides such a small surface field that no electrons are emitted. Thermionic emission is unlikely, so the magnetosphere may be empty. This would certainly account for the dearth of pulsars with periods greater than 2 s.

Endean carries this argument further in an article on page 184 of this issue of *Nature* by attempting to put the observational data on young and old pulsars into some sort of evolutionary sequence. First attempts at this will undoubtedly be shot down by observers who are in possession of so much detailed material that they can shoot down almost any interpretation. But the chief point is that a theorist who has contributed to the analysis of the magnetospheric problem is now in touch with the observations. There is a particular need for an explanation of the pattern of drifting sub-pulses, which seem to be characteristic of the older pulsars. Endean points out that this may fit the evolutionary stage just before the magnetosphere becomes a vacuum. It also fits the hypothesis that the emission takes place from close to the velocity of light cylinder.

There is still some way to go before speculation of this kind can give way to a solid theory of the pulsar magnetosphere, but it is encouraging to see speculation which takes some account of the observational facts.—F. G. S.

Miocene-Pliocene Boundary

FIJI is odd, for it contains both continental and oceanic rocks, but the concept of world-wide stratigraphical boundaries is even odder. Both are, however, critical to an understanding of the evolution of the Earth and are brought together by Gill and McDougall on page 176 of this issue of *Nature*. The oddity of stratigraphical boundaries is that they are purely conceptual phenomena, originally used in the eighteenth century to distinguish and relate one sequence of rocks to another. As such they usually reflected some particular facies of sedimentation, the boundaries being marked by either a significant change in the nature of the rocks deposited or, more commonly, by a distinct break in sedimentation during which the underlying rocks were often tilted or folded and then partially eroded before deposition of the next sequence.

Clearly, the recognition of such lithostratigraphical intervals is essential for unravelling the geological history of any one area, but problems arise when attempts are made to trace such boundaries into neighbouring areas. This is because the lithological unit clearly represents a specific interval of geological time during which that particular rock type was deposited whereas the boundaries also represent periods of geological time. Thus the boundaries of such units may, if they are recognizable at all, occur at significantly different times in closely neighbouring areas.

During the Phanerozoic, the past 550 million years, there was a great increase in the types and preservability of organisms. This has allowed the definition of time intervals at that time during which certain organisms lived. In 1810 Brongniart defined the Tertiary period as that interval during which the rocks overlying the Cretaceous Chalk of the Paris Basin were laid down ; this is the period now referred to in elementary textbooks as the Age of Mammals. This interval was subdivided by Sir Charles Lyell in 1833, using the studies of Deshayes, into four intervals, of which the Miocene was equivalent to the Middle Tertiary and was the time when rocks were deposited which contain between 20 and 40 per cent fossil molluscs of species existing today, and was therefore less (*mio*) recent (*cene*) than the Pliocene (more recent) rocks, which contain more than 50 per cent of species still living.

The problem with this form of time division is that a large number of species must be identified in order to perform the statistics. More often, therefore, a "faunizone" is recognized—a stratigraphical unit of rocks containing a specific assemblage of organisms of which a few particular fossils are usually taken as indices. The recognition of these index fossils is therefore sufficient to locate the rocks within an established biostratigraphical time sequence. Such divisions can obviously be synchronous where the organisms concerned are widespread and when new diagnostic species appear simultaneously on a world scale, but such requirements are difficult to meet because of the differing ecological restrictions on organisms. Different zonations thus grew up based on terrestrial fauna, shallow marine fauna and deep-water fauna.

The advent, principally in the 1960s, of precise dating using the radioactive decay of potassium to argon meant that the different faunal or floral divisions of geological time could be measured against an absolute time scale and that the biostratigraphical zonations could therefore be correlated with each other. The precision of dating, then about ±5 per cent, was, however, still poor, and has now improved to ±1–3 per cent where suitable rocks can be found to date. This has meant that Evernden *et al.* (*Amer. J. Sci.*, **262**, 145 ; 1964) were able to obtain provisional dates for terrestrial faunal zones in the western United States from interbedded lavas, but many Tertiary zones have only been dated on minerals extracted from tuffs or using glauconite.

On a world scale, the most useful and widespread faunal zonation is based on planktonic Foraminifera, for these microorganisms occur in all marine sequences, and components of the fauna evolve rapidly. Micropalaeontologists, such as Bandy, Berggren, Blow and Bolli, have recognized forty-one biostratigraphical zones in the Tertiary and two in the Quaternary (Berggren, *Nature*, **224**, 1072 ; 1969), although there are some difficulties in correlating between equatorial and temperate latitudes. Using this system the beginning of the Miocene is marked by the first appearance of the genus *Globigerinoides* and Cita and Blow (*Riv. Ital. Palaeontol.*, **75**, 549 ; 1969) have related the microplanktonic succession of southern Italy with the tropical zonation scheme. The absolute age of the boundary was, however, still determined by the dating of the Mt Capanne granodiorite of Elba at 7 million years, as fragments of this intrusive were found in undoubted Lower Pliocene rocks of the Italian mainland. This date alone was sufficient to upset many previous estimates, which had hitherto been more than 9 million years and mostly around 12 million years. Such an age had been consistent with the definition of the Pliocene by vertebrate palaeontologists who, since Matthew (*Bull. Amer. Mus. Nat. Hist.*, **50**, 59 ; 1929), have considered the appearance of the three-toed horse *Hipparion* to be simultaneous in North America, India and Europe and to define the start of the Pliocene. Radioactive dating of rocks in Eastern Europe and the Mediterranean suggests that *Hipparion* appeared in these regions some 11 to 13 million years ago. Such an event must be considered of parochial importance by comparison with foraminiferal zonation or even by comparison with the later regression of the sea from the Mediterranean, associated with major evaporite formations, although sedimentation continued in a few areas such as Sicily and in the Pannonian Basin of south-east Europe. It is in Sicily that the Miocene/Pliocene boundary is now defined within the "*trubi*" sequence, above the Messinian marls and gypsum.

This boundary, however, lies within the planktonic foraminiferal N18 zone, for *Sphaeroidinella dehiscens*, which marks the base of zone N19, appears a little later and the boundary is straddled by *Globigerina nepenthes*, *Globorotalia tumida*, *G. miocenica*, *G. multicamerata* and other Foraminifera of the N18 zone. Unfortunately the marls and gypsums do not afford material which can be dated radiometrically. But in the south-west Pacific, particularly in New Zealand and Fiji, the foraminiferal zones can be identified and also dated from interbedded lavas and tuffs. This has led Lienert, Christoffel and Vella (*Earth Planet. Sci. Lett.*, **16**, 195 ; 1972) to propose a date of 4.6 million years in New Zealand ; Gill and McDougall now put the boundary at 4.9 million years in Fiji.

The final test, however, has not yet been carried out, for reversals of the polarity of the geomagnetic field occur instantaneously on a world-wide scale (within some 10,000 years) and polarity changes have been delineated at 4.33, 4.41, 4.48, 4.65 and 5.10 million years (Opdyke, *Rev. Geophys. Space Phys.*, **10**, 213 ; 1972), and although both antipodean articles attempt to fit their data within this geomagnetic time scale, their information is, as yet, inadequate.—D. H. T.

Attacking Palindromic DNA

ONE of the most intriguing of the systems which *Escherichia coli* utilizes to protect itself against foreign DNA is the host modification and restriction system. Each strain of *E. coli* possesses its own particular system for imposing on its DNA a characteristic pattern of methylation. This modification takes place when the DNA is replicated, and any DNA entering the cell—for example a phage genome—which lacks the appropriate modification pattern is degraded by an endonuclease activity of the same system. The genetic characteristics of mutants in the system imply that one enzyme complex may both modify and degrade in appropriate circumstances. One of the most interesting questions about these systems is what confers the basis for their specificity, and no less than six articles in the November issue of the *Proceedings of the National Academy of Sciences* are devoted to this question.

Four of the articles concern one of the enzyme systems specified by the RTF (resistance transfer factor) of *E. coli*, which codes for the enzymes RI and RII. Enzyme RI converts the circular DNA of Simian Virus 40 to a linear form ; enzyme RII introduces multiple breaks into this alien nucleic acid. Mulder and Delius (*Proc. US Nat. Acad. Sci.*, **69**, 3215 ; 1972) have used partial denaturation mapping to locate the site(s) of the break in the circular SV40 DNA. After linear molecules have been partially denatured by alkali, the sequences rich in guanine and cytosine which remain double stranded can be distinguished in the electron microscope from the denatured single strands. By using this ingenious technique, Delius and Mulder found that the entire population of linear molecules generates essentially the same denaturation map. This implies that there is only one site at which the enzyme cleaves the circle to produce linear species.

Another way to denature SV40 DNA is to treat it with the gene 32 unwinding protein specified by phage T4, which denatures only one site in the genome. The distance of this site from the end can be measured in linear molecules, and Morrow and Berg (*ibid.*, 3365) show that it is constant in the linear SV40 DNA molecules produced by the RI restriction endonuclease. Morrow and Berg were also able to generate fixed points on the SV40 DNA by hybridizing it with the DNA of *Ad2$^+$ND1*, a hybrid between adenovirus and SV40. The region of SV40 DNA homologous to the hybrid is also always located a constant distance from the ends of linear molecules. These experiments located the cleavage site somewhere in the late gene region of SV40.

The linear molecules resulting from treatment with RI endonuclease are of more than academic interest, for Jackson and Berg (*ibid.*, 2904) have already used them to prepare circular SV40 DNA molecules which contain several of the genes of phage lambda and the galactose operon of *E. coli*. Mertz and Davis (*ibid.*, 3370), in an article communicated by Berg, now report that the linear SV40 DNA can be converted to closed circles by incubation with the enzyme polynucleotide ligase of *E. coli*. Both linear and circular oligomers are generated in addition to the closed monomeric circles.

The implication of this observation is that the restriction enzyme makes a break in each strand of the double helix at a different point, so that when the linear molecule is formed each end of the duplex has a protruding length of single strand. Because the single stranded regions at each end are complementary, they can hydrogen bond together to reform the circle and can then be covalently linked by ligase. By measuring the equilibrium constant for the joining reaction at different temperatures, Mertz and Davis deduce from the enthalpy of reaction that about 5 ± 1 nucleotides must separate the two points at which the enzyme makes its breaks.

One way for an enzyme to cleave both strands of DNA is for the recognition sites to be palindromic, so that the action of the enzyme is symmetrical with respect to the DNA base pair sequence. By studying the products of the reaction of the enzyme of *Haemophilus influenzae*, Kelly and Smith showed some time ago (*J. Mol. Biol.*, **51**, 393; 1970) that the enzyme cleaves both strands in the centre of the palindromic sequence:

5′ —pG-pT-pC/T-pA/G-pA-pC—— 3′
3′ ——Cp-Ap-G/Ap-T/Cp-Tp-Gp— 5′

Danna and Nathans (*Proc. US Nat. Acad. Sci.*, **68**, 2913; 1971) have shown that this enzyme cleaves SV40 DNA into eleven specific fragments, which may prove useful for sequencing studies.

If the action of the RI endonuclease on SV40 DNA also takes place at a palindromic site, the "heads" and "tails" of the linear molecules created by cleavage should possess the same terminal single stranded sequence. Renaturation and treatment with ligase should then yield molecules in which heads or tails have been joined to each other instead of to their original partner sequence. Mertz and Davis point out that such molecules should "snap back" instantly to form hairpin duplexes. Their observation of such structures supports this model, which demands that the enzyme must have a two-fold axis of symmetry so that it cleaves the two strands of DNA at opposite ends of a sequence such as:

A B C C′ B′ A′
A′ B′ C′ C B A

so that it must generate even numbered breaks. By comparing the number of cleavages made in different DNA substrates with the number of times any particular length of bases would occur by chance, Mertz and Davis show that the recognition site is probably six base pairs long, in which case it will occur once in every 4,100 base pairs. If the same sequence is recognized in all DNAs upon which the enzyme acts, then any two products of the reaction should join together by renaturation and treatment with ligase. These experiments therefore offer the prospect that DNAs of different types can be covalently connected into hybrid molecules.

In another article in the same issue of the *Proceedings*, Hedgpeth, Goodman and Boyer (page 3448) show by sequence studies of the termini released by the enzyme that its substrate is indeed the predicted palindromic sequence of DNA. In this case, the ambiguities in the sequence lie outside the sites of cleavage, instead of at the centre as with the *H. influenzae* recognition site. The enzyme cleaves at the asterisked points two bases from each end of the sequence:

——pA/T-pG*-pA-pA-pT-pT- -pC-pT/A —
——T/Ap-Cp—Tp-Tp-Ap-Ap-*Gp-A/Tp—

generating the cohesive ends predicted from the properties of the linear products.

The specificity of action of the RI enzyme bodes well for sequence studies on its substrates, but Horiuchi and Zinder (*ibid.*, 3220) show that the enzyme of *E. coli* B is not so selective. Phage f1 is a useful substrate for this enzyme because genetic analysis identifies two sites at which mutation can confer resistance to its degradative action. But although the enzyme does not attack phage which is mutated or methylated at these two sites, when the template is in a suitable state it appears to be cleaved at several sites. This implies that the enzyme recognizes only two sites, but that cleavage at many other sites may succeed recognition of a susceptible template. The elegant studies on the *H. influenzae* and RI endonucleases may not, therefore, apply to all of the restriction enzymes.

Turning to the modification activity of the system of *E. coli* K, Haberman, Heywood and Meselson (*ibid.*, 3138) show that the same enzyme preparation can both methylate and restrict; only S-adenosyl-methionine is needed for modification activity *in vitro*, but degradation can take place if Mg^{2+} ions and ATP are also supplied. The enzyme is a multimer and in both *E. coli* K and B it seems that in addition to this large enzyme with both methylated and restricting activities, a smaller enzyme can be found which has only the modification capacity. This prompts the speculation that it consists of the recognition and modification elements of the enzyme, but lacks the component with restriction activity. These activities are just those which are predicted by a model for the enzymatic action derived from the genetic studies of Hubacek and Glover (*J. Mol. Biol.*, **50**, 111 ; 1970).—From our Molecular Genetics Correspondent.

MYOSIN

Casting Vote

from our Molecular Biology Correspondent

It is a familiar feature in the recent history of research on muscle proteins that experiments devised to determine whether the stoichiometry of an interaction is one or two have generally given answers around 1.5. According then to whether the disposition of the authors has been to simplify or complicate the picture by some new proposition (that the myosin heads are not equivalent, for example), a choice of interpretation has presented itself. A prominent example is the question of whether or not both heads are capable simultaneously of binding actin. By the democratic criterion at least, the issue has been open, but Eisenberg, Dobkin and Kielley (*Biochemistry*, **11**, 4657 ; 1972) have now weighed in heavily in favour of the simpler answer. Their technique was to titrate polymerized actin (F-actin) with heavy meromyosin (which by virtue of its truncated shaft has more tractable solubility properties than myosin itself), and to measure the fraction remaining in the supernatant during sedimentation in the analytical ultracentrifuge, using ultraviolet scanner optics. It is important to take account in such experiments of a background of unpolymerized actin, the magnitude of which is more or less independent of the total actin concentration, and therefore probably represents a "critical" (equilibrium) concentration of monomer in the highly cooperative aggregation reaction.

The results seem to leave little room for doubt: all the heavy meromyosin is carried down with the F-actin up to a ratio of one myosin molecule to two actin monomers, after which all further myosin remains in the supernatant. The binding constant is too high to measure, regardless of ionic strength, as long as ATP is absent. The results, although agreeing with those of other recent studies, are in irreconcilable and unexplained conflict with the conclusions reached a few years ago by Young, on the basis of an essentially identical experiment. They undermine still further the rather shaky structure of evidence regarding functional differences between the two heads of the myosin molecule.

Another result that seems to go some way towards resolving an irksome ambiguity is that of Malik, Marchioli and Martonosi (*Arch. Biochem.*, **153**, 147 ; 1972), who have studied the binding of ADP to heavy meromyosin in the presence of a selection of divalent metal ions. The relevant question is how the demonstration by Taylor and his associates—that the rate-limiting process of the myosin ATPase is the dissociation of the products—is to be reconciled with the reportedly rapid rate of dissociation of ADP from its myosin complex prepared simply by mixing. The answer, it seems, may lie in the difference between the temperatures at which the two studies were done. Malik *et al.* have now performed the ADP binding experiments at 6° C, rather than 25° C, to allow direct comparison with the analyses of the ATPase, and have arrived at the happy conclusion that in these conditions the dissociation of ADP from heavy meromyosin is indeed slow enough to be comparable with the steady-state ATPase velocity.

Malik *et al.* measured first the binding constant of ADP to heavy meromyosin by equilibrium dialysis (showing, it may be remarked, a stoichiometry of just over one ligand per protein molecule, a finding on which they wisely refrain from enlarging). The rate constant of the binding (forward) reaction was measured by stopped flow, taking advantage of the small ultraviolet difference spectrum that the association generates. Dividing this into the equilibrium constant, they obtain an estimate of the reverse (dissociation) rate constant. Now the binding constant, and also the ATPase activity, vary markedly with the nature of the cation present, yet the correlation of ATPase turnover number with the dissociation rate constant of the ADP-heavy meromyosin complex extends to four of the five cations that were tried, only strontium being somewhat out of line. Both the ADP binding and ATPase level show a correlation with the size of the metal ion, but the two functions peak at different values of the ionic radius.

It is widely recognized that anomalies in enzymatic and stoichiometric properties of heavy meromyosin, as well as of isolated myosin heads (subfragment-1), are apt to arise from proteolytic damage in the course of preparation, because both forms are made by digestion of myosin with trypsin or papain. The inhomogeneity of subfragment-1 preparations is strikingly obvious in SDS-gel electrophoreses shown by Cooke (*Biochem. Biophys. Res. Commun.*, **49**, 1021 ; 1972), who advocates a new preparative procedure. This involves papain digestion of whole myofibrils, rather than purified myosin. The notion is that the heads themselves are relatively shielded against damage in the fibril, possibly by association with the actin filaments. At all events, after extraction with pyrophosphate and magnesium to dissociate active heads from the actin, followed by gel filtration, a distinctly better looking product results, at least by the electrophoretic criterion. The maximal actin-activated ATPase is also somewhat higher than that of conventional subfragment-1 preparations. On the other hand, the calcium-activated ATPase is appreciably lower than in preparations of the usual type, and this the author tries but fails to explain away. More studies perhaps are needed.

Undirectional Replication of Mitochondrial DNA

In *Nature New Biology* next Wednesday (January 24) Kasamatsu and Vinograd report a further step in the exemplary analysis of the mechanism of replication of the covalently closed circular duplex DNA of mouse cell mitochondria, a subject which has been one of the chief preoccupations of Vinograd's group these past two years. Vinograd and his colleagues have shown that the first step in the replication of mitochondrial DNA is the synthesis of an RNA chain some 450 nucleotides long which is complementary to a unique region of the so-called light (L) strand of the mitochondrial DNA. This molecule acts as a primer for the synthesis of the complementary heavy (H) strand once an endonuclease system becomes operative. The nascent daughter H strand displaces the parental H strand which then acts as a template for the synthesis of a daughter L strand.

What Kasamatsu and Vinograd have now established is that replication of this circular DNA duplex occurs in only one direction and not in both directions around the circular parental molecule. They have done this by examining in the electron microscope the position of the two forks of the replicated region of replicating double length mitochondrial DNA molecules. These molecules consist of two monomeric genomes joined in a head to tail fashion and although two RNA chains are made at the start of their replication only one acts as a template for DNA synthesis. The other simply forms a displacement loop which provides a fixed physical marker.

STEROIDS

Trial of Antiandrogen

from a Correspondent

MANY men, possibly as many as 50 per cent of those over the age of 60, suffer from enlargement of the prostate to the extent that the urethra is constricted leading to urine retention. The usual form of treatment is surgical, but, as an alternative, hormones and hormone antagonists have been used.

It is known that the male sex hormone is involved in the normal growth and functioning of the prostate and is assumed to play a part in the development of benign prostatic hypertrophy. Hormones with antiandrogenic activity have thus been used in treatment, but unfortunately most of these have disadvantages—the use of oestrogens causes feminization and the use of potent synthetic progestins usually leads to a decrease in production of testicular hormones by suppressing gonadotrophin release from the pituitary. One synthetic antiandrogen, cyproterone acetate, seems to have a beneficial effect, but, over a long period, it also seems to decrease spermatogenesis and leads to loss of libido and potency. These effects again probably result from an inhibition of gonadotrophin secretion by the pituitary.

There is also a high incidence of prostatic hyperplasia in dogs. Neri and Monahan now describe (*Invest. Urology*, **10**, 123; 1972) the effects of treating dogs with a non-steroidal antiandrogen, 4′-nitro-3′-trifluoromethylisobutyranilide. Sixteen aged dogs were given the compound orally for 6 weeks and a further three dogs were treated with the compound for 1 year at a dose level of 5 mg/kg. The volume of the prostate and the height of the epithelial cells were significantly reduced after treatment for only 6 weeks and these changes were accompanied by a reduction in the secretory function of the prostate as shown by a decrease in acid phosphatase activity and protein content of the gland and by electron microscopic studies. After 6 weeks of treatment the dense secretory bodies, vesicles and the Golgi apparatus, which were seen in the pre-treatment biopsies, were absent showing a loss of secretory function. The testes, as shown by examination of biopsies, appeared unaffected by the treatment and there had been no decrease in the level of plasma testosterone. Within 8 weeks of stopping treatment, the atrophied prostate reverted to a hyperplastic condition.

When given orally, the compound seems to be equally potent as cyproterone acetate, a steroidal antiandrogen which competes with androgens at the target organ receptors. 4′-Nitro-3′-trifluoromethylisobutyranilide, however, unlike cyproterone acetate, does not have the progestational activity which may be responsible for the pituitary inhibition, neither does it seem to have any other hormonal activity. Furthermore, it does not seem to produce any undesirable side-effects, so that results of trials in humans will be awaited with interest. Even if the results are not so striking in man as in dogs, at least they may lead to some decrease in prostatic size with an improvement in rates of urinary flow.

ENVIRONMENT

Pressure from Pleasure

from our Plant Ecology Correspondent

THE swing in ecological research towards the study of human effects on the environment became evident at a recent symposium of the British Ecological Society in Sheffield (January 2–4). As well as recurrent pollution themes the ecological problems resulting from recreational pressures on the environment received considerable attention and there is evidence that recreational ecology is passing from a descriptive phase (pioneered by Baker in 1935) to an experimental phase.

The current interest in the countryside among the general populace has led to a considerable increase in demand for access to areas which are sensitive to heavy trampling. Dr N. J. Bayfield (Nature Conservancy, Banchory) described how upland footpaths in such areas as the Cairngorms and along the Pennine Way are deteriorating seriously as a result of increasing numbers of people using them each year. One of the greatest problems is that of lateral spread of footpaths, laying bare additional areas of soil. Dr Bayfield has found that this effect increases with soil wetness, and becomes most severe in the upland bog areas of the Pennines which are particularly sensitive to trampling. Path width is inversely related to roughness of terrain, a fact which suggests that the best sites for paths are the roughest areas.

Some experimental work reported by Dr E. A. G. Duffey (Nature Conservancy, Monk's Wood) indicates that invertebrate animals are even more sensitive to trampling than are most plants. He placed plant litter in nylon bags and laid them in experimental plots on the surface of soil beneath grass. He then subjected them to two levels of trampling (60 and 120 treads per annum) for a year. The effect of the trampling was to fragment the litter and reduce the air space from 63 per cent in the control to 54 per cent and 37 per cent in the two treatments, as measured by thin sectioning of embedded material. The numbers of animals present in twenty-five litter bags were reduced by half and the number of species present by three-quarters, but there were no marked differences between the two treatments. This indicates that animal populations are being severely affected at trampling levels which are too low to affect the composition of vegetation.

Vehicles, of course, can also have a considerable and harmful effect upon vegetation. Dr M. J. Liddle (Bangor) described how vehicle tracks on sand dunes at Aberffraw, Anglesey, first

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More of the MS2 RNA Sequence

FIERS and his colleagues at the University of Ghent are continuing remorselessly to what must be their ultimate goal, the determination of the complete sequence of MS2 phage RNA. Having already determined the sequence of the coat protein cistron and part of the replicase subunit cistron, they report in *Nature New Biology* next Wednesday (January 24) the sequence of the codons specifying the last forty-five amino-acids of the assembly protein cistron and the sequence of the intercistronic divide (twenty-six bases) between the assembly protein and coat protein cistrons. Furthermore, Vandekerckhove, Nolf and Van Montag in an accompanying article report the amino-acid sequence at the carboxy terminal end of MS2 assembly protein. This amino-acid sequence is precisely that predicted from the base sequence reported by Fiers *et al.* From their analysis of MS2 RNA, Fiers *et al.* conclude that all sixty-one sense codons of the genetic code are present in this phage genome albeit at different frequencies.

Also in *Nature New Biology* next week Federoff and Zinder report about the requirement of host cell factors during the replication of Qβ RNA and f2 RNA. Federoff and Zinder find that the f2 replicase, a much less stable enzyme than Qβ replicase, requires a dissociable host cell factor when it uses both f2 viral RNA and complementary f2 minus strands as template for RNA synthesis. In the absence of this factor the f2 enzyme can, however, use poly (C) as a template for the synthesis of poly (G). Furthermore, the factor required by the f2 replicase seems to be different from those required by phage Qβ replicase when it uses Qβ viral RNA as template. The precise nature and function of these host factors in the replication of the RNA genomes of the RNA phages remain, however, to be elucidated.

cause the formation of a crust impregnated with organic matter in the surface sand. When this is fragmented by further usage, erosion results. Dr Liddle has experimented with a variety of remedial operations in the early stages of damage and has found that harrowing of the compressed surface accompanied by the addition of fertilizers significantly improves recovery by encouraging the rapid growth of meadow grasses (*Poa pratensis* and *P. annua*).

Experiments of this type may enable descriptive recreational ecology to develop into informed and effective environmental surgery.

PROVIRUSES

Site of Synthesis

from our Cell Biology Correspondent

MOST stocks of most viruses seldom contain more than one infectious particle per ten physical particles and more often contain only one infectious unit per hundred or thousand physical particles. It is therefore almost impossible to determine unambiguously how an infectious virus particle enters a cell and brings about an infectious cycle. One can, however, use the electron microscope coupled with autoradiographic techniques to observe the fate of a sample of the virus particles in a population that is allowed to adsorb to any particular population of cells and assume—this assumption is usually tacit—that the minority of infectious units behave like the majority of physical particles. Dales, Hanafusa and Huima (*Virology*, **50**, 440 ; 1972) have just done this in a painstaking way using Schmidt Ruppin Rous sarcoma virus and an avian leukosis virus (RAV 2) labelled with ^{3}H-uridine and secondary cultures of chick embryo fibroblasts. Their conclusions, in particular about the site of synthesis of the DNA provirus, are at variance with those of Hatanaka *et al.* who last year reported somewhat similar experiments with murine RNA tumour viruses and mouse cells.

Dales *et al.* allowed the virus particles in the presence of DEAE dextran to adsorb to the cells for 1 h at 4° C or 10° C during which time from 500–2,000 virions irreversibly adsorbed to each cell. Electron micrographs of these cells revealed two interesting points. First, cells comprising about 4–18 per cent of the population which have a distinct morphology different from the majority of fibroblasts adsorb many more virions than typical fibroblasts. Second, the adsorption sites at the surfaces of fibroblasts have a distinct structure ; they consist of a reticulum of fibrils and resemble gap junctions.

When cells are warmed from 4° C or 10° C to 37° C, a minority of the virions are phagocytosed and transported in phagocytic vacuoles to the vicinity of the nucleus and, by 10 min after the temperature shift, labelled RNA molecules can be detected by autoradiography in the nuclei of the cells. The amount of label in the nucleus reaches a maximum about an hour after the temperature shift, and a simple piece of arithmetic based on several not unreasonable assumptions indicates that if all the ^{3}H-uridine remains in viral RNA there must be between twenty-five and seventy-five genome equivalents per infected cell nucleus after an hour at 37° C. This, of course, is only a small fraction of the number of virions that adsorb to the cells. Aware of the problem that viral RNA may be degraded and the ^{3}H-uridine re-utilized in the synthesis of cell RNA, Dales *et al.* performed appropriate control experiments which eliminated this possibility.

Clearly the infection of chick cells by these avian tumour viruses involves the rapid transport of viral RNA to the cell nucleus, and this finding suggests, of course, that the synthesis of a DNA provirus by reverse transcription may well occur in the cell nucleus, which is what one might have predicted. But Hatanaka *et al.* have reported that soon after mouse cells are infected with mouse sarcoma or leukaemia virus, DNA synthesis can be detected by ^{3}H-thymidine autoradiography in the cytoplasm and this synthesis, they suggested, was the synthesis of DNA proviruses. By contrast Dales *et al.* apparently found no evidence of cytoplasmic DNA synthesis above background in chick cells infected with avian viruses. They therefore believe that at least in the avian system proviruses are made within the cell nucleus, not in the cytoplasm.

The complete discrepancy between the conclusion of Dales *et al.* and that of Hatanaka *et al.* merits resolution. The generous way to account for the difference is simply to suggest that the avian and murine systems are quite different, but *a priori* that seems most unlikely. Perhaps Dales *et al.* could be persuaded to repeat their experiments using murine viruses and cells.

EUTROPHICATION

Is *p*H the Clue ?

from a Correspondent

THE changes in fauna and flora—eutrophication—which result from the addition to lakes or estuaries of large quantities of inorganic nitrates or phosphates from sewage and agricultural run-off are often deleterious, especially to fisheries. The mechanisms of these changes, however, are not always clear. O'Brien and de Noyelles (*Ecology*, **53**, 607 ; 1973) now show that *p*H changes may often be implicated.

The initial response to over-fertilization is usually a "bloom" of one or more species of alga. Intense blooms are followed by the disappearance of many animal species, those with high oxygen requirements often seeming to be most susceptible. These disappearances have been ascribed to toxins produced by the algae, to low oxygen concentrations resulting from bacterial decomposition of dead algae, and to high oxygen concentrations caused by rapid photosynthesis.

O'Brien and de Noyelles applied one of three fertilization treatments to each of six experimental ponds of equal size, with two remaining as unfertilized controls. For two summers, various environmental parameters were monitored, together with the densities of plant and animal species. In the ponds with the most fertilizer, summer increases in phytoplankton were followed by disappearances of crustacean zooplankton. These disappearances occurred at different plant densities but at almost identically high *p*H values. Furthermore, water from these ponds could be detoxified by 'Millipore' filtration, which caused a slight reduction in *p*H with no change in oxygen tension.

The authors present further evidence which, though not conclusive, suggests

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Nuclear Giant RNA Contains Messenger Sequences

THERE has recently been a great deal of indirect evidence that heterogeneous nuclear RNA is a precursor of mRNA. Direct proof of this is provided in last Wednesday's edition of *Nature New Biology* (**241**, 66 ; 1973) by Williamson, Drewienkiewicz and Paul, of the Beatson Institute of Cancer Research, Glasgow. These authors report that when heterogeneous RNA with a high molecular weight from mouse reticulocytes was injected into *Xenopus* oocytes along with labelled histidine, and the soluble fraction was then analysed on a 'Sephadex G-100' column, radioactivity was located in the haemoglobin region. Material from this region co-chromatographed with mouse globin chains when examined on CM cellulose. Similar labelled material from a control experiment did not chromatograph as globin. When brain heterogeneous RNA, isolated in the presence of a reticulocyte lysate, was injected into *Xenopus* oocytes no globin synthesis occurred.

These results eliminate the possibility that aggregation of heterogeneous RNA and cytoplasmic globin mRNA had occurred during the preparation of the heterogeneous RNA fractions.

that a *p*H effect may underlie disappearance of zooplankton from "culturally enriched" waters of low buffering capacity. This disappearance would not only disrupt food chains leading to higher trophic levels (for example, fish), but would also remove predation on the algae and lead to further increases in algal density.

It would seem, though the authors do not suggest it, that if this effect is confirmed there would be circumstances in which *p*H monitoring with occasional slight manipulation could prove worthwhile "preventive medicine".

LIQUID HELIUM

No a.c. Josephson Effect

from a Correspondent

THE implication of some recent work by Musinski and Douglass (*Phys. Rev. Lett.*, **23**, 1541; 1972) is that many earlier reports which purported to describe investigations of the a.c. Josephson effect in liquid helium were in fact describing nothing of the kind. The a.c. Josephson effect is an important macroscopic quantum phenomenon predicted to occur in superfluids.

The only superfluids known are liquid ^{4}He and the electron gas in a superconducting metal, so there has naturally been a considerable incentive to compare these two systems: the analogues of phenomena observed in superconductors have been assiduously sought in liquid helium, and *vice versa.* A basic feature of superfluids is that they display long range order, that is the motions of individual particles throughout a given volume of a superfluid are very highly correlated, by contrast with the random motions of classical kinetic theory. A particularly interesting situation arises when two such volumes are weakly coupled through a very narrow channel, so that neither perfect correlation between their particle motions, nor complete independence, can be assured. Josephson predicted that if there is also a difference in chemical potential (an energy per particle) between the two volumes, then periodic flow should occur in the connecting channel with a frequency proportional to the chemical potential difference. This remarkable assertion was soon verified experimentally for superconductors, and the phenomenon has subsequently been investigated in great detail. It was always anticipated that the effect would be much harder to find in helium (chiefly because helium atoms are neutral and much heavier than electrons), so the report by Richards and Anderson (*Phys. Rev. Lett.*, **14**, 540; 1965) that they had seen the a.c. Josephson effect in superfluid helium was hailed as a considerable scientific achievement.

Richards and Anderson inverted the experiment which had originally been proposed. They coupled two baths of helium through a narrow (1.5×10^{-3} cm) orifice, forced periodic flow within it by using a beam of ultrasound, and argued that anomalies should then be seen in the relative chemical potentials of the two baths. What they actually observed was that particular values of the difference in liquid level between the two baths, corresponding to differences in their chemical potentials, remained stable for long periods of time: liquid did not flow through the orifice to equalize the levels, as would be expected classically. The stable level differences were equally spaced from each other, in agreement with theory, and the effect ceased as soon as the ultrasonic transducer was switched off. After the experiment had been improved and repeated in several different laboratories the phenomenon seemed to be well authenticated, although, as Richards himself remarked in a later report, the stable states were always disturbingly hard to find.

Musinski and Douglass have now repeated the experiment yet again, but with two extra parameters at their disposal. They were able to create a small variable temperature difference between the two baths which, like a level difference, changes their relative chemical potentials. They also used an ultrasonic transducer whose frequency could be varied. If the values of level difference where arrest of flow occurred are really determined by the a.c. Josephson effect, then they should be changed by variation of either temperature difference or frequency. In the event, Musinski and Douglass found that the level differences were almost independent of temperature difference, and that their frequency dependence was in the wrong direction. Moreover, they also noticed that the stable states were occurring at particular absolute heights in one of the baths, and were not dependent on the level difference between the two baths. The inescapable conclusion is that the stable states of zero flow observed by Musinski and Douglass were not Josephson states, but artefacts arising from the experimental arrangements. It therefore seems highly probable that Richards and Anderson, and also the several other workers who came after them, misinterpreted their experimental data and thus did not, as they believed, observe the a.c. Josephson effect. If this is the case, it must come as a considerable disappointment to all scientists interested in superfluidity.

But why did earlier workers not apply the simple tests used by Musinski and Douglass to confirm the interpretation which they were placing on their data? Why has it taken seven years to show that their conclusions were probably erroneous? The answers

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Background Radiation no longer Anomalous

FIVE years ago cosmologists were concerned to read in *Physical Review Letters* of the anomalously high values that emerged from the first far infrared measurements of the background radiation. These cast doubt on the role of the background radiation as a cornerstone in the evidence of a big-bang cosmology.

The cosmologists can now breathe again. In November last year the group responsible for the original measurements reported a repeat experiment in which no unusual flux was detected (Houck, Soifer, Harwit and Pipher, *Astrophys. J. Lett.*, **178**, L29; 1972), and next week's *Nature Physical Science* (January 22) contains a confirmatory report by a group at the Los Alamos Scientific Laboratory of the University of California.

The anomalous flux came to light in a rocket flight to discover whether the 2.7 K Planck curve describing the background radiation at radio wavelengths also applies in the submillimetre region where the blanketing effects of the atmosphere make observations difficult. It came as a surprise that the measurements showed a flux corresponding to a blackbody temperature between 4 and 6 K higher than the expected 2.7 K. Although it was almost immediately pointed out that this result is in conflict with some upper limits to the strength of the background radiation which can be obtained from studies of optical absorption lines in interstellar material, cosmologists will be relieved that rocket experiments are failing to reproduce the original findings.

The experiment carried out by the group responsible for the original result involved a telescope based on the original instrument, but with some modifications to rule out possible sources of interference which had been suggested to the authors, and the result was consistent with a 2.7 K background. This is also the result of the Los Alamos experiment, although in this case the analysis was complicated by problems encountered during the rocket flight.

There is still no explanation for the earlier anomalous flux, however. It now seems that it cannot have been of galactic or cosmic origin: the question is whether it was a consequence of some deficiency in the measuring instruments, or whether some phenomenon, possibly linked with the solar cycle, can be implicated.

seem to be that anybody who performs an experiment with the clear expectation of a certain result, and then obtains that result, can only too easily fall into the trap of being less than fastidious in eliminating ambiguities of interpretation. The moral, for all scientists, is obvious.

MOLECULAR LIQUIDS

Excitons Found?

from our Molecular Physics Correspondent

ONE of the more notable received ideas to be dispelled in recent years, as far as the physics of condensed phases is concerned, is that the existence of localized electronic excitations, or "excitons", is an essentially solid state phenomenon conditional upon the regularity and symmetry of the crystal lattice. It was not until 1966 that Rice and Jortner (*J. Chem. Phys.*, **44**, 4470 ; 1966) pointed out the obvious, namely that, with respect to distances comparable with the wavelength of the exciting radiation, simple liquids also show the required translational symmetry—in the precise technical sense that a quasi-free electron may be represented as a plane wave to an accuracy effectively unimpaired by the fluctuations in liquid structure over distances of a few atomic radii.

Almost simultaneously, Beaglehole in Chicago (*Phys. Rev. Lett.*, **15**, 551 ; 1965) obtained spectra from liquid xenon which were consistent with the existence of Wannier-type excitons, those with relatively large electron-hole separation and correspondingly weak binding. Since then the experimental side of the field seems to have been relatively static, although a burst of considerable energy was registered as Rice, Jortner and colleagues began to extend their original theoretical insights. (See, for example, Rice, Nicolos and Jortner, *J. Chem. Phys.*, **48**, 2484; 1968; Fisher and Rice, *Phys. Rev.*, **176**, 409 ; 1968.)

A new paper now raises the question of whether excitons can be observed in molecular, as opposed to atomic, liquids. Eckhardt and Nichols (*Phys. Rev. Lett.*, **29**, 1221 ; 1972) of the University of Nebraska describe measurements of the specular reflexion spectrum of pure liquid α-methylnaphthalene, in the region 215 to 400 nm, which show both the broadening and redshift, relative to the corresponding spectrum in solution, characteristic of exciton formation. The comparison is not straightforward, however, because the opacity of the neat liquid in the required region is far too high for a detailed spectrum to be observed directly in absorption—hence the need to rely on reflexion spectra from the liquid surface. To effect the comparison it is then necessary to perform a Kramers-Krönig transform on the results, thus extracting the required imaginary part of the refractive index, which corresponds to the absorption.

The authors are cautious in their ascription of the results to exciton formation, pointing out that dielectric effects in the solutions used might lead to the observed shifts and broadening, although this seems somewhat unlikely.

Nevertheless, these doubts about interpretation reflect the extent of the difficulty of establishing real contact between quantum mechanical theories of the exciton phenomenon and the optical effects which can be reliably observed. Although valuable progress has been made by the Chicago school in relating exciton scattering, and hence lifetimes and band-broadening, to simple models for the interaction in the liquid, several largely independent difficulties—for example, uncertainty about the detailed nature of small-wavelength fluctuations in the liquid, and lack of information about the distribution of excited states in even the simplest substances—combine to frustrate most attempts to calculate quantitative broadenings and shifts from fundamental quantum statistical mechanics. The advances made are nonetheless considerable, for they have established the general interrelationships between the phenomenon and other questions of vital interest such as the dynamics of polarization waves and the characteristics of translational collective modes ; the latter were introduced into the more general context of liquid theory by Zwanzig (*Phys. Rev.*, **156**, 190 ; 1967).

For the time being the outlook would seem to favour the view, recommended by Rice, that once liquid exciton formation is established it should be regarded as a particularly sensitive optical probe complementary to others now available for deriving information about time-dependent liquid structure, rather than as a problem demanding immediate elucidation through imperfect models of the liquid state. Of course, the distinction is not clear, and it is precisely for this reason that the problem is fascinating ; to an extent rather unusual among similar problems, the whole verification of the construction placed upon the experimental results, and not simply their direct explanation, is at stake in the search for an adequate theoretical model. The resulting mix of experimental and theoretical difficulties is, at all events, extraordinarily rich, made up of unsolved, yet promising, problems in spectroscopy, *N* body theory, and dielectric phenomena, to name only the principal ingredients.

SEISMOLOGY

SHOAL *versus* Fallon

from our Geomagnetism Correspondent

ALTHOUGH attempts to discriminate between earthquakes and underground nuclear explosions were given significant stimulus and emphasis by the political events of the 1960s, they were necessarily firmly rooted in academic geophysics. In recent years, however, published comparisons of the effects of explosions and earthquakes seem to have acquired an altogether more explicitly academic flavour. Clearly the two aims are far from mutually exclusive; but it is perhaps indicative of a change in emphasis that in a new study of elastic wave radiation from the two types of event Lambert *et al.* (*Geophys. J.*, **29**, 403 ; 1972) barely mention discrimination. Indeed, they are far more interested in "information about the intrinsic character of the source and the propagation medium" and parameters "of fundamental geophysical interest".

Methane and Carbide on the Moon

IN next Monday's *Nature Physical Science* (January 22), Cadogan, Eglinton, Maxwell and Pillinger report measurements of the methane and carbide contents of Apollo 11 fines. Cadogan *et al.* took samples containing sizes between 108 and 152 μm and separated them into six fractions with differing densities and magnetic susceptibilities. They find that both methane and carbide occur preferentially in those fractions which contain strongly magnetic particles, and they go on to explain this in terms of the exposure and impact histories of the individual grains.

Previous work by this Bristol group has shown that the contents of methane and carbide in lunar fines are closely related to the time for which the fines have been exposed on the lunar surface, and also that both compounds seem to reside chiefly on the surfaces of the particles. Their new measurements cause them to come out against one of the possible sources of carbide—an impact vapour cloud rich in iron and carbon. If much of the carbide in the fines were formed in this way, they say, then all particles should have a film of iron and carbide on them, and should thus be magnetic and contain comparable quantities of carbide. That is not the case.

On the other hand Cadogan *et al.* find in favour of carbide generation either by meteorite impact or solar wind implantation. Iron silicates could be reduced to iron under these circumstances and carbon already present in the particle could then be dissolved to form carbide.

To obtain this information and estimate the relevant source parameters, Lambert and his colleagues have carried out an extremely detailed and lengthy study of the surface wave radiation from two explosions and one earthquake. Their particular aims were, first, to determine from surface wave spectra the differences between the long-period radiation from earthquakes and explosions; second, to determine the spatial radiation patterns from the two types and the differences between them; and, third, to describe the individual sources quantitatively. In a comparative exercise of this kind, there is clearly some advantage in studying at least one earthquake-explosion pair with a common point of origin, common recording stations and, if possible, similar radiated energy. In this way, irrelevant phenomena and complicated corrections can be largely avoided.

The events chosen to conform most closely with these conditions were the nuclear explosion SHOAL (m_b=4.9) of 1963 and the Fallon earthquake (m_b=4.4) of 1962, both of which occurred within 60 km of each other in Nevada and both of which were recorded by the Long Range Seismic Measurement (LRSM) network. For further comparison between explosions themselves, the BILBY explosion (m_b=5.8) of 1963 was also investigated. Not only was this event of higher magnitude than SHOAL, it was detonated in tuff (by contrast with granite for SHOAL), thus enabling Lambert *et al.* to investigate variations with yield and the nature of the source medium.

The important conclusions are, first, that at long periods the surface wave radiation field from the Fallon earthquake is a quadrupole field corresponding to a quadrupole or double-couple source. At higher frequencies, however, the radiation pattern contains asymmetries indicative of multiple contributions of higher order, probably produced by the propagation of ruptures. Both these results agree quantitatively with theoretical predictions. The surface wave radiation from the explosions, on the other hand, is best explained by sources comprising a superimposed monopole and quadrupole. In the frequency range comparable to that over which the earthquake signal was recorded, there was no suggestion of multipole components of higher order. What Lambert and his colleagues regard as their principal conclusion is that the anomalous double-couple radiation from the explosions is probably not a consequence of earthquake triggering but rather of the relaxation of stress around the shatter zone generated by the shock.

The detailed comparison between the SHOAL explosion and the Fallon earthquake shows, first, that the ratio of the Love wave amplitudes (earthquake/explosion) decreases with increasing frequency. This implies a larger source for the earthquake. The second result is that, whereas for the explosions the normalized spectral ratio of Love wave amplitude to Rayleigh wave amplitude was close to one and almost independent of frequency, the same ratio for the earthquake was two to three times greater and decreased with increasing frequency. In other words, the earthquake generated Love waves far more efficiently than did the explosions and in a manner dependent on frequency. Finally, Lambert *et al.* thus conclude that these differences might be useful as discriminators between explosions and earthquakes, at least for events with m_b greater than 4.4. On the other hand, as they are careful to point out, there is no guarantee, on the basis of this analysis alone, that all earthquakes behave similarly.

RELATIVISTIC ASTROPHYSICS

State of the Art

from a Correspondent

THE Texas Symposia on relativistic astrophysics have become biennial reports on the state of the frontiers of astrophysics. During the most recent, held between December 18 and 22 in New York, some fifty speakers summarized the situation for an audience of more than a thousand astrophysicists and physicists.

The first day was devoted to quasars and radio galaxies. Professor H. Arp (Hale Observatories) opened the session by summarizing the case for a non-cosmological origin of redshifts, most of the evidence being based on detailed studies of the unusual members of the extragalactic population. This was followed by several talks given by what could be called anti-Arp forces, who prefer to place emphasis on the normal characteristics of most of this

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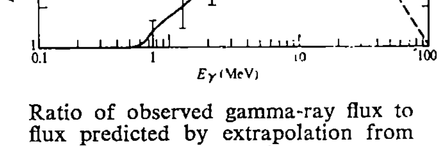
Progress in Gamma-ray Astronomy

Two contrasting contributions in next Monday's *Nature Physical Science* (January 22) emphasize the rapid development of gamma-ray astronomy in recent months. In one, Stecker reviews the present status of theory and observation concerning the diffuse cosmic gamma-ray background; in the other, Guthrie and Tademaru put forward a model to explain the presence of a low energy (473±30 keV) line in the spectrum of gamma rays from the galactic centre.

The observations of Guthrie and Tademaru stem from a balloon flight (Johnson *et al.*, *Astrophys. J. Lett.*, **172**, L1; 1972); those of Stecker are chiefly from rocket and satellite experiments, including those on OSO-3 (Kraushaar *et al.*, *Astrophys. J.*, **177**, 341; 1972) and unpublished data obtained during the flight of Apollo 15. The wide range of observational facilities now available is, of course, the underlying reason for the explosion of interest in gamma-ray astronomy, just as in X-ray astronomy.

In the case of the galactic nucleus, Guthrie and Tademaru suggest that a cluster of neutron stars may be generating the observed line through a mechanism in which electron-positron pairs are first produced in the rapidly rotating intense magnetic fields associated with a neutron star and then annihilated at the star's surface. Gravitational redshifting of the resulting radiation could then account for the difference between the observed line energy and the theoretical energy for radiation produced in this way (511 keV). Sturrock's studies of pulsars have shown that sufficient electron-positron pairs might be produced for the mechanism to be effective (*Nature*, **227**, 465; 1970), but other suggestions, including the possibility of a nuclear de-excitation line such as that from ^{7}Li (which is stable and has a line energy of 477 keV), cannot be ruled out in the present state of the art.

Stecker's article is concerned with the cosmological implications of the diffuse gamma rays, rather than with events in our own Galaxy. But again the question of matter-antimatter interactions arises. With the new gamma-ray observations, there is an essentially complete spectrum of the background radiation from 10^{-3} to 100 MeV. Above 1 MeV, the gamma-ray spectrum no longer follows the power law typical of X-ray energies, and the ratio of observed flux to extrapolated flux reaches a maximum of 10 near 20 MeV (see diagram). One way in which additional gamma rays might be produced between 1 and 100 MeV is by matter-antimatter annihilation, with a peak at around 70 MeV Doppler shifted to lower frequencies by expansion of the universe. Again, there are many other possible interpretations of the data; but this must be one of the most intriguing possibilities, suggesting the presence of large amounts of antimatter in the universe which is able to interact with the matter there.



Ratio of observed gamma-ray flux to flux predicted by extrapolation from X-ray energies.

population, and conclude that some, and probably all, redshifts are cosmological. Dr L. Woltjer (Columbia University) aptly summarized the attitude of many astrophysicists towards Arp's evidence by saying "it is difficult to believe, but I am still worrying about it".

An independent thread running through the first day was the problem of possible super-relativistic velocities in the radio sources 3C 279 and 3C 120. Dr K. Kellermann (National Radio Astronomy Observatory) pointed out that there are many ways of interpreting the data which do not require "super-c" velocities, particularly using models with components in the source blinking on and off; this interpretation was strongly emphasized by Dr W. Dent (University of Massachusetts). Dr I. Shapiro (Massachusetts Institute of Technology) said that, although radio experiments testing general relativity have not yet distinguished between the Einstein theory and the Brans-Dicke theory, radio observations may yet resolve the question.

The second day was devoted to the experimental and theoretical aspects of gravitational radiation. Dr J. Tyson (Bell Laboratories) did not provide supporting evidence for Weber, but emphasized that Weber's work has resulted in so much growth in the technology for detecting gravitational radiation that definitive experiments, whether negative or positive, may soon settle the problem. A "hot" discussion of the subject erupted in the middle of the scheduled programme a couple of days later when Professor J. Weber (University of Maryland) stated an impromptu "theorem" to the effect that there are an infinite number of incorrect ways of conducting experiments for detecting gravitational waves. He suggested that other workers should more closely follow his methods which have been "proven" to produce results. Tyson and others responded rather spiritedly, and on the whole negatively, to Weber's suggestions.

The esoteric theoretical aspects of gravitational radiation were discussed by Dr R. Geroch (University of Chicago), Professor R. Penrose (University of London), and Professor C. Misner (University of Maryland). Their chief topics were, first, the question of whether considerable energy could be extracted from interactions with singularities (black holes), and, second, whether such singularities would be "naked" or "clothed" (that is, special circumstances could allow radiation to escape from inside a singularity).

On the third day Professor F. Pacini (Laboratorio Nazionale di Frascati) and Professor F. Drake (National Astronomy and Ionospheric Center) reported on the state of the theory and observations of pulsars. Although some clarifications have occurred and some observational dogmas discredited, the advance of the subject has not been as great as was once hoped.

The striking impact of X-ray astronomy on relativistic astrophysics was evident in the reports of Dr R. Giacconi and Dr H. Tananbaum (American Science and Engineering). The most exciting subject of the symposium concerned the unusual X-ray, optical, and radio events occurring in close binary stars. Tananbaum's discussion of the X-ray eclipsing system Her X-1, and the report by Professor N. Bahcall (Princeton University) on its probable optical counterpart, HZ Herculis, revealed exceptionally interesting data on a binary system which eclipses in both the optical and the X-ray regions of the spectrum, has both short and long term on-off cycles, shows effects of X-rays heating a probable A star to make it appear much hotter on one side, produces pulses by containing a compact object with a "hot spot" rotating every 1.24 s, and shows a host of other interesting details.

The theoretical aspects of X-ray double stars were discussed by Dr K. Prendergast (Columbia University) and Dr D. Pines (University of Illinois). Professor B. Paczynski (Warsaw Institute of Astronomy) summarized what is known about the evolution of close binaries and gave a warning about well known traps awaiting people who interpret data on close binaries too simply. Dr R. Hjellming (National Radio Astronomy Observatory) discussed the radio phenomena associated with both close binary stars and X-ray stars, emphasizing that unusual high energy phenomena must be associated with both types of objects. The workshop on black holes found several supporters for the "almost invisible" component of Cyg X-1 as the currently known object likely to be a black hole.

Details of the X-ray close binaries (Cen X-3, Her X-1, and Cyg X-1) were discussed by Professor R. Ruffini (Princeton University); in particular he considered whether the compact objects that must be present are black holes or "ordinary" neutron stars. The sense of the discussions was that, because of effects by which a star of lower mass could mimic one of higher mass, it was probably not yet safe to declare that Cyg X-1 contains a black hole. The case for this is, however, improving, and in the near future one may be able to say a black hole has been "observed".

The last day of the symposium consisted of talks by Dr R. Omnes (High Energy Laboratory at Orsay) and Dr S. Frautschi (CalTech) about physics at the origin of time, and several talks on miscellaneous subjects, of which the first reports of X-ray observations with Copernicus presented by Dr P. Sanford (Mullard Space Science Laboratory) and the report by Professor A. Penzias (Bell Laboratory) on the first detection of deuterium in interstellar space were perhaps the most interesting. Penzias reported that deuterium was found in the Orion nebula through detection of radio lines from the molecule DCN; the abundance of deuterium is roughly an order of magnitude greater than expected.

MARINER 1977

Experiments Chosen

EXPERIMENTS planned for the two Mariner missions to Jupiter and Saturn, to be launched in 1977, have been divided into eleven groups, NASA announced recently. The two craft will be identical, although they may follow slightly different trajectories, and will use the gravity field of Jupiter to accelerate them past Saturn; this mission is the remnant of a more ambitious "Grand Tour" plan for one or more spacecraft each to visit all the outer planets by repeated use of this gravitational slingshot effect. That has now been abandoned, even though a suitable alignment of the outer planets occurs only once every 179 yr.

The two missions now proposed will carry instruments for:

- Optical imaging of Jupiter, Saturn, their moons and the rings of Saturn.
- Radiofrequency studies of Saturn's rings, the atmospheres of both planets and of interplanetary space.
- Infrared studies of the planets; this will assist in determinations of atmospheric composition.
- Ultraviolet spectroscopy.
- Magnetometer investigation of the interplanetary magnetic fields as well as those of the two planets.
- A plasma experiment to study the interaction of the solar wind with the planets.
- Analysis of low energy cosmic rays and particles in the radiation belts of the planets.
- Investigation of high energy (interstellar) cosmic rays.
- An experiment to determine velocity and range of interplanetary and interstellar particulate matter.
- Photopolarimetry of the atmospheres of the planets and investigation of reflective properties of their moons and Saturn's rings.
- Studies of the non-thermal radio emission of the planets, their plasma resonances and magnetospheres.

The flight will take four years, covering 807×10^6 mile, and will be planned in detail in the light of the preliminary investigation by Pioneer 10 of deep space and the region near Jupiter.

Do Honey Bees have a Language?

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Von Frisch and later adherents of the theory that honey bees communicate by means of an elaborate dance are challenged by controlled experiments which show that their data can be explained in terms of olfactory cues.

WHENEVER new data and interpretations are presented which cannot be reconciled with established beliefs, it is proper and desirable that supporters of the traditional view should examine these data and interpretations with great care, and offer such objections as can be generated. In 1969, on the basis of studies of the recruitment of honey bee foragers to food sources, we compared the predictive powers of the classical "language" hypothesis of von Frisch[1] with those of a simple olfaction model for forager recruitment and concluded that olfaction provides the best interpretation of our data[2].

Investigators who believe that honey bees have a language have since challenged our conclusion[3–5], and two other recent articles[6–7], while not including a discussion of our results, cannot be reconciled with our interpretations. Our purpose here is to examine the principal objections to our interpretations and present additional data.

Procedure and Results

From earlier experiments, we knew that scent fed into a hive on one day influences forager recruitment on the next. We established a hive and a line of three experimental sites, each 200 m from it, in a dry field. The sites were approximately 150 m apart and the prevailing light breeze never blew towards or from the hive. Instead, the wind moved from site 1 to site 3, with site 2 in the middle.

During experimental periods of three hours, we fed scented sucrose to ten marked regular foragers at each of sites 1 and 3. Recruited bees were captured and killed. On a following day we fed unscented sucrose at sites 1 and 3 and planted scented sucrose at site 2, which had not been visited by bees from our hive. In this situation, the language hypothesis predicts that recruited foragers would be captured at sites 1 and 3, both visited by successful foragers from the hive. If, however, recruited foragers locate food sources by olfaction, they should arrive at site 2 which was not visited by any bees from the hive.

In four repetitions of this experiment (on days 2, 7, 12 and 16) we captured a total of twenty-five new recruits at site 1, 224 at site 2, and eight at site 3. Thus, newly recruited foragers had located a site in the field not previously visited by them or their hivemates, and had failed to arrive at locations about which they should have been well informed (according to the language hypothesis).

When foragers are experienced at a food site, they are again recruited to it by odour cues rather than by language[8,9] and, when odour cues are rigorously excluded, recruitment of new foragers fails[2,10]. For example, on control days of our experiments reported in 1969 when no scented sucrose was made available (days 4, 9 and 14), arrival of recruits at our feeding stations was drastically curtailed[2]. As a further control, we allowed ten bees to fly to each of four unscented feeders for 3 h (July 25, 1968) for a total of 1,374 round trips. During this period only five recruits from a hive of 60,000 bees found the feeders[2].

Thus, both experienced and inexperienced foragers seem to require olfactory cues to locate a food source in the field. In the absence of compelling evidence to the contrary, it is conservative to suggest that olfaction alone is sufficient to account for recruitment of honey bees to a food source.

Objections to Our Model

In spite of his polemic, Dawkins[3] does offer one substantive objection by arguing that bees are easily distracted from their "intended" (linguistically communicated) goals. In this view, the bees which arrive at site 2 have been distracted from sites 1 and 3, a possibility which deserves serious consideration. But in our experiment, site 2 was downwind from 1 and upwind from 3. Is it likely that recruited foragers could be simultaneously distracted upwind and downwind from their intended goals, or that any animal can be attracted to a downwind odour source? In any case, when all three sites were provided with unscented sucrose (days 9 and 14), recruits failed to arrive at sites about which they were supposedly linguistically informed[2]. We conclude that Dawkins's "distraction" model is not supported by the data.

Esch and Bastian[6] reported interesting new data but did not relate their findings to the literature on forager recruitment. In each of their experiments, a group of bees was trained to feed at a scent-marked site near the hive, and ten of the foragers were marked and confined temporarily in a cage. The feeder was next moved to a new location 200 m from the hive and the number of regular foragers reduced to one marked bee. The ten marked former foragers were then released and observed, to discover whether they would be re-recruited to the scent-marked feeder at the new location, as they should be on the hypothesis of linguistic communication by dance attendance.

Fourteen of seventy experimental bees did attend dances and subsequently found the new feeder location. Nineteen additional marked bees attended dances and flew from the hive without arriving at the feeder. The remaining thirty-seven marked experimental bees had no contact with the dancer and did not fly to the new location of the feeder.

Ten of the fourteen successfully re-recruited bees required between one and nine exploratory flights with intermediate contacts with the dancer. Only four succeeded on the first flight, two of them within 1 min of flight time. Many of the nineteen unsuccessful dance attenders also made several flights from the hive; they attended between five and thirty-one dances (mean, 17.5) and made between one and nine exploratory flights (mean, 3.4), without finding the feeder.

For the fourteen successfully re-recruited bees the mean time in flight between first attending the dancer and locating the feeder was 8.5 min, compared with less than 0.5 min for experienced foragers[11]. Esch and Bastian did not report the durations of flights by unsuccessful dance attenders.

In spite of these negative results, Esch and Bastian consider that their data support the language hypothesis. Because four bees found the feeder on their first flights, it is inferred that, "since they could not have searched the entire experimental area in such a short time . . .", successful re-recruits must have had prior knowledge (obtained from the dance) of the feeder location.

By focusing attention on the performance of successful bees Esch and Bastian have failed to recognize that most of their data actually contradict the predictions of the language hypothesis. The population of experimental animals must be viewed as a whole. In reality, there was a total of 100 exploratory flights by marked bees after attending the dancer. If recruited bees simply flew out equally in all directions from the hive, like spokes in a wheel, 2% would be headed within 7° of the feeder location, a result which is consistent with the observations of Esch and Bastian.

More generally, the data obtained by Esch and Bastian do not bear out the claim by von Frisch[12]: ". . . the tail-wagging dance makes known the distance and the compass direction to the goal. . . . This description of the location enables the newcomers to fly rapidly and with certainty to the indicated flowers, even when these are kilometres away . . . an accomplishment on the part of the bees that is without parallel elsewhere in the entire animal kingdom". Nor do they eliminate the alternative possibility, that re-recruited foragers were flying about, using wind and odour, while seeking the scent to which they had been trained.

The article by Gould, Henerey and MacLeod[7] contains many data not available earlier, but some of their data do not fall in line with what one might expect from the dance language hypothesis. As in the study by Esch and Bastian, their experiments were ". . . designed to examine the behaviour of individual recruits as each attended a dance and subsequently arrived at a feeding station". In their series 1 experiment, marked bees were trained to two feeding stations 120 m distant from and in opposite directions from the hive, and many workers in the hive were given individual marks. During experiments, of 277 potential recruits observed to attend dances, 240 failed to arrive at any station, and only thirty-seven were subsequently captured at the feeding stations. Of these, a third arrived at a station in a direction opposite to and 240 m distant from that "indicated" in the dance manoeuvre. This result contradicts the prediction of the language hypothesis that all thirty-seven of the successful recruits should have arrived at the "correct" station.

These investigators also found that successful recruits spend a considerable amount of time in flight before reaching the food source. The direct line flight time between hive and a feeding station located at 120 m is less than 25 s[11], and recruited bees generally fly from the hive within a minute and a half after leaving a dancing bee (50% leave within 30 s)[13]. The data in Table 4 of Gould *et al.*[7] reveal that the twenty-five bees which did arrive at the "correct" station flew an average of more than thirty times longer than would be necessary to "fly rapidly and with certainty" to the food source. The twelve bees which ended up at the station in the opposite direction averaged only thirty-six times as long as necessary for a direct flight.

A greater number of marked bees arrived at the station regularly visited by the foragers which recruited them than to the one 240 m from it, and some successful bees found the food source quickly (two in less than a minute), so Gould *et al.* concluded that quantitative information was communicated by the dance. The authors thereby focus attention on successful performers as did Esch and Bastian.

In another experiment, these authors fed sucrose of high molarity at one station and very low molarity at the other. Most of the dancing in the hive was by foragers regularly visiting the high molarity food source; and during the experiments most of the recruits captured were at that location. This correlation is accepted by the authors as evidence of linguistic communication.

As Gould *et al.* carefully pointed out, the validity of their interpretations for both of the above experiments depends upon the assumption that perfect odour symmetry existed between the two stations. In experiments of this type even small asymmetries of location odour do influence recruitment[13]. Gould *et al.* located their stations in aromatic vegetation. They got uniformly high recruitment whether or not they added scent to the food, yet there is considerable evidence that recruitment is minimal to an unscented location[2,10]. The high recruitment they obtained indicates that the feeding locations had odours detectable by bees. The unanswerable question is: Did asymmetries of these odours exist between two feeding locations 240 m apart?

Mautz[5] also was concerned with the behaviour of individually marked workers which came in contact with a forager dancing in the hive. In his experiments, 32% of marked workers that attended dances found the feeder, and the amount of time the potential recruits attended the dancer was positively correlated with success at finding the food. In addition, the average flight time for successful recruits was more than ten times that expected of experienced foragers and the mean flight time of bees which flew out but failed to find the feeder was twice that of the successful recruits. Mautz noted that one bee found a goal at 400 m after following only five waggle cycles of the dance.

As with Gould *et al.*, and with Esch and Bastian, Mautz assumed that his feeder locations were not recognizable by bees as olfactorily distinctive and that only linguistic information could be communicated more effectively by increased duration of contact with the dancer. He does not discuss the possibility that a recruit which spends more time attending a dancing bee might, by so doing, gain a more accurate impression of the odour characteristics of a specific location. Again we see a supporter of the language hypothesis focusing attention on the successful recruits.

Of the several papers we review, Lindauer's[4] was the most deliberate and direct effort to obtain data contradictory to our findings. The first type of experiment undertaken by Lindauer resembled those of Gould *et al.*[7] in design, and yielded similar data. Forager bees were trained from a hive to two feeding sites, and were then fed high molarity sugar at one and low molarity sugar at the other. Virtually all dancing was by bees visiting the high molarity sugar site, and most successful recruits landed there. Lindauer assumed, as did Gould *et al.* and Mautz, a perfect symmetry (to bees) of environmental odours at his locations. From this he inferred that, "if the recruits followed only the odour signals given by the dancers . . . they should have appeared in equal numbers at (both) sites". In accordance with his assumption Lindauer attributed the asymmetry in recruit arrivals to linguistic communication. Thus, the untested assumption of station symmetry (to bees) is central to the reasoning of Lindauer as well as to the above authors.

In his second experiment, Lindauer put out three stations in a geometry similar to that used in our experiments[2] and trained bees to stations 1 and 3 but not to 2. Then, with scented sucrose at all three stations (a variation from our design), he collected recruits. Although the stations were deliberately asymmetrical (no foragers at station 2), approximately one-fourth of all captured recruits arrived at station 2. The language hypothesis predicts that the recruits should have travelled only to stations 1 and 3.

In order to reconcile these data with the language hypothesis Lindauer generated *ad hoc* the auxiliary hypothesis that potential recruits alternate their attentions between dancers visiting sites 1 and 3, and subsequently "integrate the directions communicated by both groups of foragers".

Although the "integration" model satisfies Lindauer as an explanation of his data, it could not possibly predict the distribution of recruits in our earlier experiments[14,15] or, indeed, in the recent experiments of Gould *et al.*[7].

Lindauer got good recruitment at his stations 1 and 3 when presenting unscented food at those locations. Interpreted in the light of our data[2,10] these results suggest that Lindauer's feeding sites were in some measure distinctive to bees. This may explain the asymmetry of recruitment he observed when foragers to station 1 were killed and bees visited only a single station. Unfortunately, the precise location and ecology of the sites for these experiments are not given in his paper (except that it was near Frankfurt), nor does he provide dates, wind speed and directions, number and sequence of observations contributing to the total data and other relevant information. These omissions make any interpretation difficult and speculative. Another portion of Lindauer's paper offers some philosophical and rhetorical objections to our paper, but we will consider these later.

Thus all the authors we have discussed[4–7] explicitly or implicitly assumed that the feeding stations they established in the field were in no way distinctive to bees and that the environment can be made symmetrical with respect to odours and other factors. They also assumed that, in order to find the food, a recruit must have prior quantitative information about its location. These assumptions lead the authors to interpret arrival of new workers at sites visited by dancing foragers as definitive evidence of linguistic communication. As pointed out earlier they have focused their attention on successful recruits. Experiments based on these assumptions invariably lead to affirmation of the consequence of the hypothesis (if bees have a language, recruits will reach the food. Some recruits find the food. Therefore, bees have a language). This reasoning is deductively invalid[19].

The experimental designs of these investigators suffer yet another serious disadvantage. It is not logically possible experimentally to establish the validity of the station symmetry assumption (failure to display asymmetry does not prove that none exists). It is quite practical, however, to seek positive evidence of station asymmetry in experiments of this design. One way would be to remove all directional information from dances performed by foragers regularly visiting food sites. If, in spite of this, recruits preferentially arrive at the feeder regularly visited by the foragers which recruited them, it could be concluded that they had done so without use of prior directional information, and that honey bees can exploit subtle environment asymmetries in the recruitment of new foragers to food sources.

We have incorporated the use of "directionless" dances in the design of the experiments reported below.

Conditions and Observations

In the summer of 1970 we did experiments using a single frame observation hive and two feeding stations located 150 m from it in approximately opposite directions (west and east of the hive, but slightly north of it). The hive and stations were located at the University of California, Santa Barbara. Both stations were located in dry fields, devoid of green vegetation. The West Station was nearer the sea and upwind ; the East Station somewhat closer to the University buildings. Otherwise, the sites appeared to be symmetrical.

Ten marked foragers were trained to feed at each station ; all successful recruits were either killed or marked as replacements for regular foragers which were then killed. Observations were made at the hive and stations during 3-h periods (0830–1130), August 21 to September 4, 1970, and food was provided only during those periods. A westerly breeze prevailed during this period (up to 5 mile h^{-1} on most days) and the usual temperature was 65°–75° F.

A principal objective of the experiments was to examine relationships among food molarity, forager behaviour, and recruitment. Therefore, scent added to the food was held constant. All solutions used were scented with lavender oil (32 μl. l.$^{-1}$). Sucrose solutions of 0.8 M, 1.3 M, 1.8 M and 2.3 M were used. On any given day a solution of lower molarity was offered at one station and one of higher molarity at the other. Rotation of molarities between the stations controlled for possible inherent differences in location attractiveness, and on each day the stations acted as controls against each other. The experiments were run blind: the observers were not informed of molarities of sucrose provided at the feeding stations on any given day.

The hive had glass sides and was equipped with a clear plastic atrial chamber inside a diffusely lighted observation room. Hive conditions (well populated, and with little natural forage) ensured that our marked foragers danced in the atrial chamber, rather than on the comb. These dances were on a horizontal surface, and contained no discernible directional information. The straight (waggle) portions of the dance were apparently randomly oriented and highly variable within each dance episode.

Altogether, a total of 1,793 dances by our marked bees and 136 dances by unmarked bees foraging on natural sources were observed during eleven days (33 h) of experimentation. Thus, during our study periods, 93% of all dancing in the hives was by our marked foragers.

Although we were largely successful in eliminating oriented dances from our hive, occasionally a marked forager did enter and perform a dance episode on the vertical surface of the comb. These occurrences will be of great interest to proponents of the language hypothesis, so we will present data on oriented dances before proceeding to other aspects of the study.

There was a total of only 50 apparently oriented dances recorded during 33 h of experimentation ; 1.5 such dances h^{-1}, on the average, or approximately 2.8% of all dance episodes recorded for our marked foragers. These occurred equally (24 to 26) for the two stations and did not correlate with recruitment (Table 1).

These oriented dances were not distributed evenly throughout the experimental period, but occurred sporadically. For example, 40% of them occurred on one day, August 30, 1970. Occurrence of a block of oriented dances on a given day did not appear to influence recruitment. A comparison of data for August 30, 1970 (which had the greatest number of on-comb dances during the eleven days of experimentation) with the following (more typical) day is illustrative, and is presented as Table 2.

Table 1 Dances by Unmarked Bees, Oriented Dances, Disoriented Dances, and Recruitment

	First hour	Second hour	Third hour	Total
Dances by unmarked bees	77	38	21	136
Oriented dances by marked bees	23	9	18	50
Disoriented dances by marked bees	337	675	731	1,743
Successful recruits	64	115	143	322

Data are partitioned according to time of occurrence in our experiments. Total data for 33 h of observation are presented.

Table 2 Comparison of Visitation by Marked Foragers, Oriented and Disoriented Dances by Marked Foragers, and Successful Recruitment of New Bees for August 30, 1970 (with many Oriented Dances) and August 31, 1970 (with few)

	Trips by marked foragers		Oriented dances		Disoriented dances		Successful recruits	
	1.3 M	1.8 M	1.3 M	1.8 M	1.3 M	1.8 M	1.3 M	1.8 M
August 30, 1970	319	267	9	19	76	110	20	65
August 31, 1970	304	312	1	2	59	143	19	67
Total	623	579	10	21	135	253	39	132

Table 3 Mean Number of Trips by Marked Foragers; of Disoriented Dances by those Foragers; and of Successful Recruits per 3 h Observation Period for 0.8 M, 1.3 M, 1.8 M and 2.3 M Lavender Scented Sucrose Solutions

Molarity	Forager trips	Disoriented dances	Successful recruits
0.8	308	26	5
1.3	320	86	19
1.8	293	117	42
2.3	231	107	17

Not less than four or more than seven observation periods at each molarity.

Table 1 also shows that dancing by unmarked bees foraging on natural food sources declined as the experiment progressed. This is consistent with our findings that insertion of a new food source in the hive-environment system may change the behaviour of bees regularly foraging on an established one[10]. Presumably this alteration is mediated through a change in the available recruit pool.

From our data on oriented dances (Tables 1 and 2) it is not possible to infer that these dances are responsible for the observed recruitment of new foragers to those feeders we had established in the field. There is, however, a positive correlation between the number of disoriented dances (or total dances) and recruitment of new foragers (Table 3).

The experimental design is not rigorous enough to define the asymmetry in environmental cues used by recruits while searching for and locating a particular feeder in the field, but quantitative directional information does not appear to be a part of that system.

While doing this set of experiments, we also gathered information on Nasanov gland exposures at the food source by bees foraging on various molarities of sucrose. Our previous studies indicate that Nasanov gland exposure by regular foragers fails to attract undisturbed bees but apparently does provide a point of reference for disoriented members of the colony. Gland exposure is apparently a function of the interest potential recruits may have in a food source, rather than food quality *per se*[2,10]. Nasanov gland exposure by foragers visiting established food sources in the field was depressed at the lowest molarity we used (Table 4), a fact which indicates that few recruits were in the field searching for that source.

Further Considerations

We have done several experiments which were designed to determine whether honey bees use linguistic communication under defined conditions[2,8,9,14–16]. Results indicated that the language hypothesis has little heuristic value and fails as a predictive tool. The results further suggest that if one wished bees to pollinate a particular crop, it should be useful to regulate the odour carried into the hive by foragers, rather than the angle of dance on the comb.

More generally, we feel that honey bee foraging ecology is regulated by a complex system of hive, environmental and behavioural variables. With sufficient knowledge, it should be possible to manipulate the system and predict the consequences for the foraging ecology of a honey bee colony. We then might say that we understand colony function in terms which are neither teleological nor anthropomorphic; and we would be in a position to attack pragmatically problems of a comparative or practical nature. Accordingly, we have examined interrelationships among Nasanov gland exposure, visits of marked foragers to a food site, dancing in the hive, and recruitment of new foragers, and correlated these with the amount of odour in sucrose solutions provided in the field. In these experiments we have had some success in manipulating the system[10], as have Waller[17] and Friesen[18].

Table 4 Relationships Among Molarity of Sucrose Solutions Provided, Forager Visitations, and Nasanov Gland Exposures by Marked Foragers

Molarity	Forager trips	Nasanov gland exposures
0.8	308	24
1.3	320	77
1.8	293	85
2.3	231	71

Means for 3 h observation periods are given (7 ≥ periods/molarity ≥ 4).

Waller showed that association of odours with food in the field, but not odours alone, could increase bee populations in experimental plots[17]. Friesen examined interrelationships among wind speed and direction, forager flight paths, odour levels and locations, forager visitation and recruitment of new foragers to sites in the field. He concluded that, after recruits leave the hive, their success and distribution depend upon an interaction of field variables affecting the distribution of odours[18]. Thus, evidence from several sources indicates that odour is of great importance in the system of variables which regulate honey bee foraging ecology.

Our comparison of the predictive values of the olfaction and language hypotheses of honey bee forager recruitment was an attempt to determine just how important odour is in this system[2]. To our surprise, our results and interpretations generated a controversy which deeply polarizes interested biologists. Along this line we must stress that the controversy does not emerge from a difference of opinion about the acceptability of various parts of a body of evidence.

The ingenious step and fan experiments of von Frisch have been repeated many times, and our own published data clearly show that when his procedures are closely followed, without insertion of additional controls, distributions of successful recruits may be expected to resemble those obtained by him[14,15]. Similarly, when Lindauer used an experimental geometry modelled after ours, he obtained data consistent with ours[4]; and the data presented in Table 3 of this paper resemble those obtained by Gould *et al.* and by Lindauer when they used similar experimental designs[4,7]. Neither the repeatability of experiments on honey bee behaviour nor the care and accuracy with which workers in this field gather and report data appears to be in question.

Proponents of the language hypothesis argue that the many repetitions of the von Frisch experiments make it highly probable that his interpretation is correct. One must realize, however, that the amount of additional confirmation affected by each new favourable repetition of an experiment becomes smaller as the number of previous repetitions grows[19]. Thus, even under the most favourable conditions, sheer number of repetitions is never sufficient to render a hypothesis immune to challenge. Furthermore, in the case of the bee language hypothesis, the existence of a considerable body of unfavourable evidence greatly diminishes the weight of even a large body of confirming data[20].

Any hypothesis which is generated as an explanation of certain observed events will, of course, imply their occurrence. The events to be explained will then be taken as supporting evidence for it. If the hypothesis is valid it also may lead to *a priori* predictions of facts and events in conditions different from those leading to its formulation.

It is exactly here that we have difficulty with the language hypothesis of honey bee orientation. Each time we have inserted previously omitted controls or altered the experimental design to create new test implications, the distribution of successful recruits to feeders located in the field is no longer that predicted by the language hypothesis. Similarly, much of the evidence recently obtained by Esch and Bastian, by Mautz, by Gould *et al.* and by Lindauer is contrary to the predictions of that hypothesis[4–7].

The difficulties we had in reconciling our data[14–16] with the language hypothesis led us to propose the alternative olfaction model[21,22]. The olfaction hypothesis allowed a satisfactory explanation of the distribution of successful recruits in those experiments which incorporated new controls[14–16] and could encompass the large body of existing data on honey bee forager recruitment. Furthermore, it had the advantage of simplicity.

Thus, in 1967 we had two hypotheses, olfaction and language, each generated *a posteriori* to explain an existing body of evidence. The language hypothesis had been well articulated by von Frisch twenty years earlier[1], but it had been expanded and modified through the years in an attempt to explain newer results. Olfaction, while new in the sense that it challenged the then currently accepted hypothesis and two decades of thought habits, was essentially a return to the position held by von Frisch and others in the earlier years of this century.

Lindauer not only presented new data but challenged our interpretation on philosophical grounds when he invoked Aristotelian (Darwinian) teleology as an argument in favour of language. He argued that in nature "each morphological structure and behavioural act is associated with a special function. On this basis alone, it would seem unlikely that information contained in the waggle dance of a honey bee is not transmitted to her nest mates"[4]. We have answered his challenge in part by discussing the relevant data in terms of philosophy of science which we consider to be more powerful[19,20].

An inherent weakness of Lindauer's teleological argument can be illustrated by giving one interesting example from another field of biology. Methyl eugenol is extremely attractive to male oriental fruit flies. In one test in Hawaii 1,300 male *Dacus dorsalis* were attracted a half-mile upwind to a muslin screen that had been treated with it. Methyl eugenol is not produced by the female fruit flies nor does it attract them. It is not a component of the natural food of this fly and probably has no nutritional value. Yet male oriental fruit flies are irresistibly attracted to it and "apparently cannot stop feeding when they have free access to it, and they kill themselves with over indulgence"[23]. Their behaviour under these circumstances certainly cannot be construed as adaptive.

Admittedly, this is an extreme example of non-adaptive behaviour, but it does reveal a weakness in the teleology argument. The mere presence of a characteristic behavioural pattern in an animal cannot be construed as purposeful, adaptive or "associated with a special function".

Lindauer[4] also challenged us on grounds that we have not individually discussed three specific situations investigated earlier by von Frisch and his colleagues. First, at distances quite close to the hive, recruited foragers may be captured at scented dishes other than the one visited by the foragers which recruit them, while at distances of 100 m and beyond "the recruited workers all fly in the direction of the feeding plate". That the latter part of this quoted statement does not hold is well documented by the data of Gould *et al.*[7] as well as by ours[2,14,15], and even by Lindauer's own data[4] unless one is willing to accept his "integration" model. As for the first part of the statement, when the feeding dishes are close to the hive, we agree with von Frisch and Lindauer; the bees seem to be using odour.

A second situation involves disoriented dances performed by foragers on a horizontal surface. In an experiment using a tilted hive, von Frisch got approximately equal recruitment in four directions while regular foragers were fed in only one direction. Later that day, with the hive put upright again, he got preferential recruitment in the direction of the feeder visited by foragers[12]. We prefer a design in which two or more stations visited by bees simultaneously serve as controls against each other, and we set up our experiment accordingly. Our data on the effectiveness of disoriented dances (Table 3) seem to be in disagreement with those of von Frisch. During our 11 days of observation, new recruits preferentially arrived at the sites visited by dancing foragers even though there was no directional component in the dances.

The third situation involves the detour of foragers around an obstacle to a feeder on the other side of it. In one experiment performed by von Frisch, marked foragers were trained to fly around a rocky ridge to a scented feeder. Scent plates were placed on top of the ridge and 50 m laterally to the direct line between hive and feeder. During a 90 min period, three new recruits were captured at the lateral stations, eight on top of the ridge and twenty-three at the feeder. Because the new recruits apparently failed to follow the flight path used by the foragers which recruited them, von Frisch feels that they were linguistically informed of the feeder location[12].

We must argue that the flight paths and duration of searching by the twenty-three successful recruits are not known, and that a failure of bees to use the detour (if indeed they did not use it) does not differentially support either language or olfaction. Since neither hypothesis predicts that recruits will follow the same path as the marked foragers, the experiment is not crucial and the results do not support or refute either hypothesis.

We believe that experimentation does not "prove" or "disprove" hypotheses, but rather affects their credibility. If the credibility of a hypothesis at any given time is determined by the total body of relevant information available, then the language hypothesis of forager recruitment was very credible in 1946 when von Frisch proposed it. It is less so now, for the body of relevant information is quite different and includes much unfavourable evidence. In fact, it is so much less credible that we no longer can believe that honey bees communicate linguistically.

Do honey bees have a language? That is a question which may never be answered with certainty. It may be more useful to examine assumptions critically, state hypotheses and their consequences with precision, review the evidence objectively, and ask: can we now believe that honey bees have a language? Thus, it appears that the honey bee forager recruitment controversy is not about the nature of evidence but rather about the nature of hypotheses[25]. It is not what investigators observe (the data) but what they believe (infer) that is at the heart of the controversy.

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Biostratigraphic and Geological Significance of Miocene-Pliocene Volcanism in Fiji

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Dating of Fijian volcanic rocks enables an estimate of $4.9\pm0.4\times10^6$ yr to be made for the age of the Miocene–Pliocene boundary. The change in composition of the volcanism in Fiji between about 5 and 6×10^6 yr ago may result from migration of the site of subduction.

ESTIMATES of the age of the Miocene–Pliocene boundary have ranged widely over the past decade from about 13×10^6 yr to 3×10^6 yr. This large spread arises partly because of problems in finding appropriate rocks to date by isotopic methods, and partly because of difficulties involved in stratigraphic and palaeontological correlations. Definition of planktonic foraminiferal zones[1] has facilitated global correlations. The Miocene–Pliocene boundary defined in Italy lies within zone N.18 and this zone has been recognized in certain stratigraphic sequences in the South Pacific.

We have used the K–Ar method to date some volcanic rocks from Fiji that are related stratigraphically to sediments containing diagnostic Neogene planktonic and benthonic foraminifera. Volcanic rocks in island arcs are inherently difficult to date by the K–Ar method because they are often porphyritic, because they may have formed under modest to high partial gas pressures, and because much of the potassium occurs in a groundmass which often contains considerable glass. The first two factors increase the likelihood of obtaining spuriously old ages due to the presence of extraneous or initial radiogenic Ar. The third factor makes it difficult to establish firm criteria by which to predict whether or not samples containing apparently undevitrified glass will give ages that are correct or only minimum estimates.

The samples used in this study are from collections by Gill[2] and Tarling[3]. All samples were examined in thin section before dating; those that showed more than incipient alteration were rejected. Analytical results and other appropriate information are presented in Table 1. Our analytical methods have been described elsewhere[4].

Age of Volcanogenic Units for Viti Levu, Fiji

Rocks of the Mendrausuthu Volcanic Group crop out in south-eastern Viti Levu and primary descriptions of them appear in several bulletins of the Fiji Geological Survey Department[5–7]. This group has been interpreted[8] as a "volcanogenic unit" composed of undeformed lavas and auto-brecciated agglomerates which grade laterally into conglomerates, greywackes, mudstones, and marls[9]. The geochemistry and genesis of the parental volcanics (the Namosi Andesite) will be discussed in detail elsewhere (J. B. G., in preparation), as have the faunas of the related sedimentary rocks[5,6,10–15]. The more distal facies include the Veisari Sandstone and the Suva Marl, which contain particularly rich faunas with planktonic foraminifera indicative of zones N.17, N.18, N.19. Basal sediments of several formations within this group contain detritus of plutonic rocks which are thought to be 9 to 11×10^6 yr old[16]. From these data the volcanism and volcaniclastic sedimentation are usually assigned to the late Miocene to earliest Pliocene. But the faunal evidence is internally inconsistent and was summarized as such by Ibbotson[6], who nevertheless favoured a late Miocene age. Ladd[11], Whipple[13] and Ladd (personal communication) maintain that the Suva Marl belongs to the Tf and probably $\mathrm{Tf}_{1\text{-}2}$ stage of the East Indies classification. The $\mathrm{Tf}_{1\text{-}2}$ letter stage is regarded as middle Miocene, equivalent to zones N.9 to N.12 (refs. 17, 18) and older than 12.5×10^6 yr (refs. 17, 19). Rodda (ref. 20 and personal communication), on the other hand, interprets the foraminifera as indicating either a Tg stage biocoensis together with reworked fossils from underlying strata, or that the larger foraminifera were contemporaries with planktonic foraminifera of zones N.17 to N.19. Ladd (personal communication) regards the larger foraminifera in question as too well preserved and abundant to have been reworked.

The same internal inconsistency seems to occur within the Futuna Limestone of the nearby Lau Islands, Fiji. This formation has been considered to be lower Tf stage and correlative with the Suva Marl on the basis of these same larger foraminifera and molluscs[20–22]. But the planktonic foraminifera which dominate certain horizons[23] are indicative of zones N.18 and N.19 (particularly *Globorotalia* (G.) *multicamerata* [=G. *menardii* var *fijiensis*], *Globigerina conglomerata*, and *G. bulloides*). Discordant K–Ar results[2] suggest that underlying volcanics are 5 to 9×10^6 yr old but these might be minimum ages only.

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We have dated three whole rock samples of Namosi Andesite and hornblende separates from two of these rocks. The ages are all concordant at 5.7±0.1×10^6 yr (Table 1), providing strong evidence that this is the age of eruption and crystallization of these rocks. Each sample has phenocrysts of labradorite and hornblende set in a fine-grained, holocrystalline groundmass of plagioclase, hornblende, an opaque and clinopyroxene. Samples 69–874 and 69–875 are clasts from agglomerate near Namosi village, whereas sample 68–66 is from an intrusive stock which forms a satellite volcanic centre (Mau quarry) about 10 km south-south-east of the others. The exact stratigraphic relationship between these samples and the Suva Marl and Veisari Sandstone horizons from which the above-mentioned fossils were collected is not known with any precision. But hornblende-bearing volcanics occur only at the stratigraphic top of the Namosi Andesite formation[5,20]. R. Todd has identified a siltstone from above or associated with the uppermost volcanics in this formation as belonging to zone N.18 (P. Rodda, personal communication). She also found *Sphaeroidinella dehiscens* in the Veisari Sandstone, a lateral equivalent of the Namosi Andesite and Suva Marl, within which there is detritus from the satellite volcanic centre represented by sample 68–66 (ref. 5). Thus by studying these three Namosi Andesite samples we believe that we have dated volcanism which occurred during the time represented by a portion of zones N.17 to N.19 and the Tg letter stage, at or near the Miocene–Pliocene boundary. Tarling[3] found five samples collected from the same site as sample 68–66 (his site 4) to be reversely magnetized.

We also dated hornblende separated from a coarse grained hornblende gabbro sample collected from a stock in Wainikaro Creek. The measured K–Ar age of 6.1±0.5×10^6 yr (Table 1, 69–870) supports the interpretation of Band[5] that the stock is cogenetic with the Namosi Andesite, rather than older as suggested by some other data[16].

Table 1 Potassium–Argon Ages on some Whole Rocks and Minerals from Viti Levu, Fiji

Sample No.	Material	Tarling[3] site No.	K (wt.%)	Rad. ^{40}Ar (10^{-10} mol/g)	$\frac{100\ \text{Rad.}\ ^{40}\text{Ar}}{\text{Total}\ ^{40}\text{Ar}}$	Calculated age (×10^6 yr±2 s.d.)	Magnetic polarity[3]	Rock type and locality
			A. Namosi Andesite; Mendrausuthu Volcanic Group (no stratigraphic relationships known)					
68–66	Whole rock	4	1.126, 1.137	0.1151	64.7	5.71±0.10	R	Andesite*, Mau quarry, 178° 14′ E, 18° 11′ S
68–66	Hornblende	4	0.314, 0.315	0.0326	20.9	5.80±0.34	R	
69–874	Whole rock	—	1.349, 1.351	0.1390	18.1	5.77±0.19	—	Dacite*, Wainanggara Creek, 178° 7′ E, 18° 3′ S
69–874	Hornblende	—	0.288, 0.283	0.0291	18.1	5.71±0.32	—	
69–875	Whole rock	—	1.653, 1.644	0.1632	23.9	5.55±0.18	—	Andesite, same site as 69–874
69–870	Hornblende	—	0.330, 0.328	0.0356	9.7	6.1±0.5	—	Diorite*, Wainikaro Creek stock, 178° 13′ E, 18° 2′ S
			B. Mba Volcanic Group (in stratigraphic sequence)					
69–894	Biotite	—	7.593, 7.587	0.593	62.6	4.38±0.06	—	Banakite* or "biotite trachyandesite", Mbasala Creek, 177° 52′ E, 17° 32 S
72–472	Whole rock	50	1.644, 1.652	0.1146	42.0	3.90±0.10	N	Absarokite, Nandarivatu Rd., alt. ~620 m
72–473	Whole rock	51	1.529, 1.529	0.1149	29.3	4.22±0.10	N	Absarokite, Nandarivatu Rd., alt. ~570 m
72–474	Whole rock	51	1.289, 1.297	0.1045	18.6	4.53±0.19	N	Absarokite, same site as 72–473
68–73	Whole rock	54	3.358, 3.349	0.2640	85.7	4.42±0.06	R	Shoshonite*, Nandarivatu Rd., alt. ~400 m

* Indicates full chemical analysis available in refs. 2, 10 or 43. $\lambda_e = 0.585 \times 10^{-10}$ yr^{-1}; $\lambda_\beta = 4.72 \times 10^{-10}$ yr^{-1}; ^{40}K/K$= 1.19 \times 10^{-2}$ atom %.

The Koroimavua Volcanic Group is a second volcanogenic unit[8,25,26] and crops out in western Viti Levu. Faunal data are much less abundant but Blow[1] assigns tuff sample PEK/F.4 to zone N.18, so that this group is also regarded as having been deposited at or near the Miocene–Pliocene boundary. The group is underlain by strata thought[10] to be no older than upper Miocene. Comformably underlying sample PEK/F.4 are the lava flows and agglomerates previously known as the Sambeto Volcanics. Biotites separated from two specimens collected about 800 m apart gave concordant K–Ar ages of 5.35±0.1×10^6 yr (ref. 27). Two biotite separates from a nearby monzonite plug, thought to be an associated volcanic centre, yielded ages of 4.9±0.1×10^6 yr. Tarling[3] found three samples (site 45) collected near those dated by McDougall to be normally magnetized.

It is salutary to note that when McDougall[27] reported these K–Ar data for the Koroimavua Volcanic Group he questioned the palaeontological dating for the sediments because it was believed at that time that the age of the Miocene–Pliocene boundary was firmly established at 12 to 13 m.y. This age for the boundary was obtained from correlations of isotopically well-dated mammalian faunas of North America into the European stages. Subsequent data from marine sequences have rendered this earlier correlation increasingly questionable.

A third volcanogenic unit, the Mba Volcanic Group, occupies the northern portion of Viti Levu and is the best-studied geologically because of its associated Au-Ag-Te mineralization at the Tavua centre[28–30]. Distal greywackes contain foraminifera loosely correlated[26] with the Tg and Th letter stages and include the planktonic species *Globigerina nepenthes* which became extinct late in zone N.19 (ref. 1). Rocks of the Mba Volcanic Group conformably overlie those of the Koroimavua Volcanic Group where they are locally in contact[20,26]. The volcanic rocks themselves have been subdivided into five phases[30].

Our four whole rock samples from the Mba Volcanic Group were collected by Tarling[3] from a section of apparently conformable lava flows separated by pyroclastics which crop out along the road between Waikumbukumbu and Nandarivatu. But Rodda suggests (unpublished) that some of these bodies may be intrusive rather than extrusive. The sites span a vertical distance of about 240 m and all belong to the oldest period of Mba volcanism (phase 1) from the Tavua centre. Their relationship to the distal foram-bearing sediments is not known. They contain phenocrysts of olivine and clinopyroxene with some plagioclase and an opaque. The olivines are partly altered to iddingsite, and minor zeolite occurs along pyroxene boundaries in samples 72–473 and 72–474. The groundmasses are holocrystalline and generally fresh, and include plagioclase, K-feldspar, clinopyroxene, an opaque, and some ($<2\%$) zeolite. These four samples define a sequence of events occurring between 4.4 and 3.9×10^6 yr ago (Table 1). Gale (in ref. 3) reported a $4.3\pm0.2\times10^6$ yr K–Ar age for one sample from Tarling's site 53, stratigraphically intermediate between our samples 68–73 and 72–474. Rodda *et al.*[16] published K–Ar ages of $\sim7.5\times10^6$ yr (minimum age, whole rock) and $10\pm0.5\times10^6$ yr (biotite) for two samples from levels 16 and 10, respectively, of the Emperor Gold Mine at the Tavua centre. We also dated biotite separated from what is locally known as "biotite trachyandesite", which represents the youngest phase of Tavua volcanism (Table 1, sample 69–894). Its age of $4.38\pm0.06\times10^6$ yr is older than those of some of the whole rocks discussed above which by stratigraphic criteria[30] should be older. Rodda *et al.* (ref. 16, sample X.27) reported a $4.7\pm0.2\times10^6$ yr age for biotite collected from the same outcrop. They also reported five other ages between 5.0 and 4.3×10^6 yr for whole rock or separated biotite samples from horizons younger than phase 1 volcanics. The 7 and 10×10^6 yr results clearly are anomalous. The rest of the measured ages lie between 3.9 and 5.0×10^6 yr and are slightly discordant. Nevertheless these data indicate that Tavua volcanism probably was confined to the interval between about 5 and 4×10^6 yr ago.

The Miocene–Pliocene Boundary

The Miocene–Pliocene boundary must be considered within the framework of the classic Neogene stratigraphy of Italy. Selli[31] discussed the upper Miocene Messinian stage and defined a neostratotype which is overlain by the "trubi" marl of the Zanclian stage, widely accepted as lower Pliocene. Using this definition, Blow (ref. 1, p. 418; also his Fig. 19) regards the Miocene–Pliocene boundary as lying within foraminiferal zone N.18, just below the base of zone N.19. This latter zone is defined by the first evolutionary appearance of *Sphaeroidinella dehiscens* which occurs in the section chosen by Selli[31] about 13 m above the base of the 65 m thick "trubi" marl, or about 13 m above the level of the type Miocene–Pliocene boundary.

The Fijian data presented here are among the few radiometric ages available for samples that are closely associated with sedimentary sequences assigned to foraminiferal zones which straddle this boundary. Our Namosi Andesite samples dated at 5.7×10^6 yr are lateral equivalents of the Veisari Sandstone and Suva Marl, samples from which have been placed in zones N.17, N.18, and N.19 by Blow[1] and Parker[15]. Significantly, some of the stratigraphically lowest samples contain *Sphaeroidinellopsis subdehiscens*, the ancestor of *Sphaeroidinella dehiscens*, which itself appears high in the sequence. Unfortunately, stratigraphic information with which to relate the various formations of the Mendrausuthu Volcanic Group or the various fossil sites with the Suva Marl and Veisari Sandstone to one another in detail has not been published. Both the Namosi Andesite and the Koroimavua Volcanic Group (which has measured biotite ages of 5.3×10^6 yr) are, however, each overlain by at least one sample which has been assigned to zone N.18. Volcanic detritus from an outlying Namosi Andesite centre also dated at 5.7×10^6 yr is interbedded with N.19 foraminifera. Because the Miocene–Pliocene boundary lies near the top of zone N.18, we conclude from these Fijian data that its age is no older than 5.7×10^6 yr and is equal to or slightly younger than 5.3×10^6 yr.

This requires that the larger foraminifera mentioned earlier are either from considerably older horizons within the Mendrausuthu Volcanic Group, or are reworked, or lived until upper Miocene time, at least in Fiji. The larger foraminifera are found in horizons stratigraphically between samples assigned to N.17 and N.18 (Rodda, unpublished), which excludes the first alternative. There is no morphological evidence for the second possibility, and the third disagrees strongly with the correlations of Clarke and Blow[18], Adams[32] and Berggren[17]. Thus the larger foraminifera seem the least definitive of the available biostratigraphic indices and their occurrence in association with 9 to 11×10^6 yr old plutonic detritus in the Mendrausuthu Volcanic Group is compatible with all the correlations offered by Berggren[17], rather than favouring his third alternative.

There are few other radiometric age measurements which are directly relevant to the Miocene–Pliocene boundary as defined in marine sequences. Micas from granitic rocks on Elba Island yielded K–Ar and Rb–Sr ages of 6 to 7.55×10^6 yr (ref. 33). Sediments exposed nearby on the mainland of Italy contain gravels, fragments in which are thought to have been derived from Elba. The stratigraphic level at which the gravels first occur is earliest Pliocene (Tabianian) (ref. 34), so that the Miocene–Pliocene boundary must be younger than the isotopic age of the granites. Tongiorgi and Tongiorgi[34] suggested that the boundary lies between 6 and 7×10^6 yr, an interpretation tentatively accepted by Funnell[35]. Nevertheless these data are consistent with a younger age for the boundary as postulated above. In Morocco, Charlot *et al.*[36,37] found K–Ar ages of 8 to 6.6×10^6 yr for micas from tuffs interbedded with sediments correlated with the Messinian stage, giving support to the view expressed by Tongiorgi and Tongiorgi. A number of K–Ar dates are available for younger Neogene samples from marine sequences in western North America but there are difficulties interpreting these results because of major internal inconsistencies discussed principally by Bandy and Ingle[38] and Bandy *et al.*[39].

In studies of microfossils from deep-sea cores, magnetic stratigraphy and the standard polarity time-scale can be used to provide physical age control. Hays *et al.*[40] record a major faunal change at about 3.0×10^6 yr ago within the Mammoth reversed event, at which level *Sphaeroidinella dehiscens* increases greatly in abundance. Bandy *et al.*[39] refer to this as the "*Sphaeroidinella dehiscens* datum" and believe that it is the level for the N.18/N.19 boundary and for the Miocene–Pliocene boundary. In contrast, Hays *et al.*[40] prefer to follow the criterion of Blow[1] in which the first evolutionary appearance of *S. dehiscens* marks the base of zone N.19, and that the Miocene–Pliocene boundary is a little earlier than this level. They show that *S. dehiscens* occurs at the bottom of core V24-59 and must have appeared earlier than 4.5×10^6 yr ago. Dymond[41] reported a $4.3\pm0.3\times10^6$ yr K–Ar age for acidic volcanic glass occurring stratigraphically above N.18 material in core from the experimental Mohole[42]. Accepting the results of Hays *et al.*[40] and combining them with our Fijian data we infer that the Miocene–Pliocene boundary lies between 4.5 and 5.3×10^6 yr ago, and we suggest a best estimate of its age as $4.9\pm0.4\times10^6$ yr. Berggren[17] adopts 5.0×10^6 yr as the age of the boundary, based on estimates by Hays *et al.* for the time of first appearance of *S. dehiscens* in deep-sea cores, which level Berggren refers to as the "*Sphaeroidinella dehiscens* datum".

Future coordinated work in Fiji may make it possible to integrate for this period the planktonic foraminiferal zones with the East Indian letter stages, K–Ar ages for interbedded volcanics, and the geomagnetic polarity time-scale. Our dated samples are not pristine or numerous enough, the palaeomagnetic data are too limited, and our stratigraphic knowledge is not sufficient to make this correlation in detail at the present time.

Geologic Significance of the Fijian Volcanism

In Table 2 we present average compositions of volcanic rocks from the three Fijian volcanogenic units we have discussed. Gill[43] noted that volcanism on Viti Levu ceased to be predominantly intermediate in character at the end of the Miocene. During the time interval we have dated, volcanism changed from calc-alkaline (Namosi Andesite) to shoshonitic (Koroimavua and Mba Volcanic Groups). A similar change occurred elsewhere in Fiji on Vanua Levu and in Lau where Pliocene volcanism produced transitional olivine basalts. Table 2 also includes an average composition of olivine basalts from Taveuni where volcanism occurred as recently as 2,000 to 700 yr ago (E. Frost, personal communication).

Table 2 Average Chemical Analyses of Some Miocene to Recent Volcanic Rocks from Fiji

	Namosi Andesite formation	Koroimavua Volcanic Group	Mba Volcanic Group	Taveuni
$N=$	8	12	12	7
SiO_2	58.4	51.0	51.0	48.3
TiO_2	0.7	0.7	0.7	1.8
Al_2O_3	17.4	18.2	16.2	17.5
Fe_2O_3*	7.0	8.7	9.6	10.0
MnO	0.2	0.2	0.2	0.2
MgO	3.4	4.3	6.2	7.1
CaO	7.5	9.6	9.5	10.5
Na_2O	3.9	3.4	2.8	3.3
K_2O	1.2	3.4	3.4	1.0
P_2O_5	0.2	0.5	0.5	0.4
Rb	21.	60.	79.	21.
Sr	545.	1,270.	1,180.	474.
Ba	388	624.	680.	290.
Pb	4.	8.	9.	2.
Th	1.7	1.5	1.3	2.5
U	0.6	0.8	0.6	1.0
Zr	99.	48.	46.	142.
Hf	1.2	1.1	1.2	—
Ni	8.	13.	60.	104.
Co	19.	25.	33.	40.
Cr	19.	26.	148.	260.
Sc	18.	21.	26.	28.
V	192.	280.	27.	230.
Cu	78.	190.	162.	61.
Y	22.	19.	17.	33.
La	10.	12.	12.	—
Yb	1.4	1.6	1.7	—
$^{87}Sr/^{86}Sr$	0.7037	0.7041	0.7038	0.7035

* Total Fe as Fe_2O_3.

Summarized from analyses by Gill[2,10,43].

Gill and Gorton[44] attributed this change in magma composition to alteration of plate configuration in the Fiji area. They argue that until the late Miocene the Lau-Colville Ridge (of which the Fiji islands are pinnacles) was underthrust from the east by the Pacific plate, but that at about the time corresponding to the Miocene–Pliocene boundary this subduction site began to migrate to the east away from Fiji. Karig[45] and Sclater *et al.*[46] have called attention to the youthfulness of the Lau Basin which today separates the Lau-Colville Ridge from the Pacific plate subduction site. DSDP drilling in 1971 has confirmed the Pliocene age of this basin[47].

Thus the change in magma composition shown in Table 2 accompanied trench migration and illustrates two effects of trench migration on the physical properties controlling magma genesis: First, volcanism became more basic (predominantly shoshonitic and basaltic instead of andesitic); second, the basic magmas changed from being initially shoshonitic (at least in places) to being nepheline-normative, lherzolite-bearing alkali basalts. The latter change brought with it higher concentrations in the alkali basalts of Ti, Zr, Nb, Hf, U, Th, and light REE, lower concentrations of K, Rb, Cs, Sr, Ba, and Pb, and higher Na/K ratios[2]. These two changes are presumably due to the gradual cessation of underthrusting beneath Fiji and, therefore, to the removal of a source of heat as well as water and/or siliceous magma. Mantle presently beneath the Lau-Colville Ridge is seismically normal whereas that presently beneath the Lau Basin is characterized by low velocities and high attenuation[48]. The change in magma composition may coincide with reversion of "anomalous" island arc upper mantle to "normal" intraplate upper mantle. In Fiji this change seems to have commenced shortly before the time corresponding to the Miocene–Pliocene boundary, and had a pronounced effect on the amount and composition of accompanying magmas.

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Comparison between Mice Chimaeric and Heterozygous for the *X*-linked Gene *tabby*

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A comparison of tail banding patterns between mice chimaeric and heterozygous for the *X*-linked gene *tabby* shows considerable differences between the two. The implications for the Lyon hypothesis of *X* inactivation and for clonal hypotheses of development are discussed.

ACCORDING to the single-active-*X* (or inactive-*X* or Lyon) hypothesis[1,2], every female mammal heterozygous for a gene carried on the *X* chromosome contains two genetically distinct cell populations, each expressing one only of the two contrasting alleles. The inactivation event which differentiates the two populations is postulated to be random, and much discussion[2-7] has centred around the question of whether the orderly phenotype displayed by many of these heterozygotes is consistent with an initially random event.

Mice containing two genetically distinct cell populations, each expressing one only of two contrasting alleles, can be manufactured by the technique of embryo aggregation[8-10]. Here the existence of two populations is, a matter not of hypothesis but of experimental design. If such an aggregation chimaera, with components carrying different *X*-linked alleles, were to display a phenotype like that of the corresponding heterozygote, it would show conclusively that the observed pattern could be generated by two populations of cells, and the principle of scientific parsimony might suggest that two populations of cells existed in the heterozygote also.

We have therefore made aggregation chimaeras between strains of mice homozygous for the *X*-linked gene *tabby* (*Ta*/*Ta*) and for its normal allele (+/+), and compared them with heterozygous (*Ta*/+) females. *Tabby* was chosen because it has provided the subject-matter for much of the previous controversy[4,6], and because its phenotype in both heterozygous and homozygous (or hemizygous) condition has been exceptionally well described[4,5,7,12]. The aggregants were mated to determine germ cell chimaerism; the gross appearance of the coat was recorded and photographed; and observations were made after death (as in 5,12) on the tail rings, the papilla vallata of the tongue, the Meibomian glands on the eyelids, and the plicae digitales on the paws. Control mice (+/+, *Ta*/*Ta*, *Ta*/−, *Ta*/+) were similarly studied. No study of the hairs was made, because this aspect has been investigated on a parallel series of aggregation chimaeras[15]. The teeth have been described elsewhere[16].

Of the eleven adult mice derived from embryo aggregation, four showed no evidence of chimaerism in any of the characters examined. The other seven (two females, five males) were overt chimaeras of which two produced mixed progenies, three only + gametes and two only *Ta* gametes. In gross appearance, two out of seven were indistinguishable from *Ta*/+ heterozygotes. Three others were mostly of heterozygous appearance, but two of these had an apparently homozygous "*Ta*/*Ta*" area, lighter in colour and lacking guard hairs, on one flank, while the third had a small area on the left side where the stripes appeared light on dark rather than *vice versa*, suggesting a higher concentration of *Ta*/*Ta* cells. One other was mostly normal ("+/+"), but with a few definite tabby stripes on the back, and the last was mostly "*Ta*/*Ta*" but with some stripes on the back and a few macroscopically visible short hairs on the tail.

Table 1 Some Effects of the Tabby Gene in Normal Mice, Tabby Heterozygotes and Homozygotes, and Tabby←→Normal Chimaeras

Genotype	No. of animals	No. showing normal morphology for: Papilla vallata	No. showing normal morphology for: Plicae digitales	Mean No. of glandulae tarsales	Mean No. of tail rings ± s.e.*
(C57BL × C3H/Bi) F_1	7	7	7	10.9	77.96 ± 0.91
Ta←→+ (wild-type)†	3	3	3	10.3	62.50 ± 0.87
Ta/*Ta*, *Ta*/–	12	0	0	0.0	74.70 ± 0.68
Ta←→+ (tabby)†	1	0	0	0.0	72.50
Ta/+	12	6	5	4.7 ± 0.9	75.19 ± 1.37‡
Ta←→+ (chimaeric)†	7	4	1	3.8 ± 1.8	70.69 ± 1.11‡

In order that all comparisons should be on an agouti background, embryos from the tabby stock maintained in this laboratory[11] were paired at the eight-cell stage[14] with agouti (C57BL × C3HBi) F_1 embryos. Controls, which like the chimaeras were fully adult at the time of killing, included homozygous *Ta*/*Ta* females and hemizygous *Ta*/– males, heterozygous *Ta*/+ females, and +/+ (C57BL × C3H/Bi) F_1 animals.

* Tail rings were counted under a × 12.5 dissecting microscope. Four counts were made over a standard 3.5 cm length, two by one observer and two by another, and the results for each animal were averaged.

† Mice derived from embryo aggregation.

‡ For this comparison, $t_{17}=2.55$, $P\sim0.02$.

Table 2 Tabby Phenotype of 11 Mice derived from T←→+ Embryo Aggregation, Grouped into 5 Grades According to the Amount of Tabby Expression in the Coat

Phenotype of coat	No. of animals	No. showing normal morphology for: Papilla vallata	No. showing normal morphology for: Plicae digitales	Mean No. of glandulae tarsales	Mean No. of tail rings	Germ cells*
Normal	3	3	3	10.3	62.50	+(14, 24, 100)
Between normal and heterozygous	1	1	0	9.7	66.25	+(86)
Heterozygous	2	2	1	2.9	70.50	+(10), *Ta* (50) Ta (26)
Between heterozygous and tabby	4	1	0	2.7	71.89	+(15, 17) +(1), *Ta* (8) Ta (46)
Tabby	1	0	0	0.0	72.50	Ta (15)

* Germ cells were classified from phenotypes of progeny from matings with *Ta*/*Ta*, *Ta*/– or +/+ partners. Numbers in parentheses indicate the number of germ cells of each type classified for each individual. This coincides with the total number of progeny for tested females, and the number of female progeny for tested males.

In tabby mice (*Ta*/–, *Ta*/*Ta*), the plicae digitales (transverse skin folds on the digits) and glandulae tarsales (Meibomian glands opening onto the eyelids) are absent or greatly reduced, while the papilla vallata on the tongue is represented only by a slit. Grüneberg[12] reported that the *tabby* gene was fully recessive with respect to the plicae digitales, in that the heterozygotes could not be distinguished from the homozygous normal animals. In our material (Table 1) the gene was not completely recessive with respect to the plicae: seven out of twelve heterozygous females showed some degree of tabby expression in seventeen out of their twenty-eight paws. The heterozygotes showed a very variable but always reduced number of glandulae tarsales, and for the papilla vallata, which was scored as an all-or-none character, some of the heterozygotes showed the normal and some the tabby condition. The four non-chimaeric aggregants resembled the corresponding tabby and wild-type control groups in respect of plicae digitales, papilla vallata and glandulae tarsales.

The chimaeras resembled the heterozygotes in having a reduced and variable number of glandulae tarsales, and in showing some individuals with the tabby condition of the papilla vallata, as well as some normals. The chimaeras differed from the heterozygotes, however, in showing a significantly higher incidence of reduced plicae digitales similar to those of the tabby controls or intermediate (thirteen out of twenty-four paws in six out of seven animals). In both chimaeras and heterozygotes, the fore-paws more often showed reduced plicae than the hind paws. Variation in size of the plicae in the apparently "normal" chimaeras and heterozygotes was not measured. Table 2 gives data on the eleven aggregants arranged according to the phenotype of the coat.

The width of the tail rings was assessed by counting the number in a standard length (Table 1), and the distribution on the tail of scales, hairs and pigment was examined. The tabby heterozygotes did not differ significantly from the homozygous normal group, nor from the tabby homozygotes. Grüneberg[5] reported that *Ta*/+ heterozygotes had significantly more (that is, narrower) rings than normal mice; our failure to find a consistent difference probably reflects the difference in genetic background[17] between the two studies. The mice derived from embryo aggregation showed significantly fewer tail rings than the heterozygotes ($P<0.01$) or the homozygous tabbies ($P<0.01$): the reduction in tail-ring number was shown most strongly by non-chimaeric aggregants (Table 2), so it cannot have been due to chimaerism. A maternal effect on tail ring width has been reported[18–20], so our result can probably be attributed to a uterine influence exerted by the Q-strain foster mothers. A similar maternal effect on number of lumbar vertebrae also proved to be exerted *via* the uterus[21,22]. The normal genotype appears to be more susceptible than the tabby genotype to the uterine influence on tail ring width (Table 2: regression of tail ring number on coat phenotype grade, $b=2.87\pm0.47$, $P<0.001$).

The pattern of scales, hairs and pigment distribution showed striking and consistent differences between groups. The normal mice showed regular rows of scales (forming the tail rings), with long straight hairs growing in bunches of three, one bunch per scale (Fig. 1*a*). The pigment, contained in melanocytes, was distributed throughout the scale, except for a pigment-free area at the posterior border of each scale, giving an overall impression of light bands on a dark background. The tabby heterozygotes (*Ta*/+) showed equally regular rows of scales (Fig. 1*b*); the hairs were thinner and less straight than in the normal animals, though still arranged in bunches of three; the pigment was less in amount and was restricted to the centre of the scale, leaving a pigment-free area at the anterior as well as the posterior border, so that the overall impression was of dark bands on a light background. Thus the heterozygous and homozygous normals both showed regular patterns, though they were readily distinguishable from one another. The tabby homozygotes (*Ta*/−, *Ta*/*Ta*), on the other hand, showed little or no regularity of pattern. The scales were arranged in rows, but these were irregular, and the pigment was widely and irregularly distributed (Fig. 1*c*), making the tail rings hard to count. A few small single, twisted hairs were present, but most of the tail was bald. The non-chimaeric aggregants showed an identical appearance of scales, hairs and pigment to that of their respective control groups, suggesting that these features are not influenced by the uterine environment.

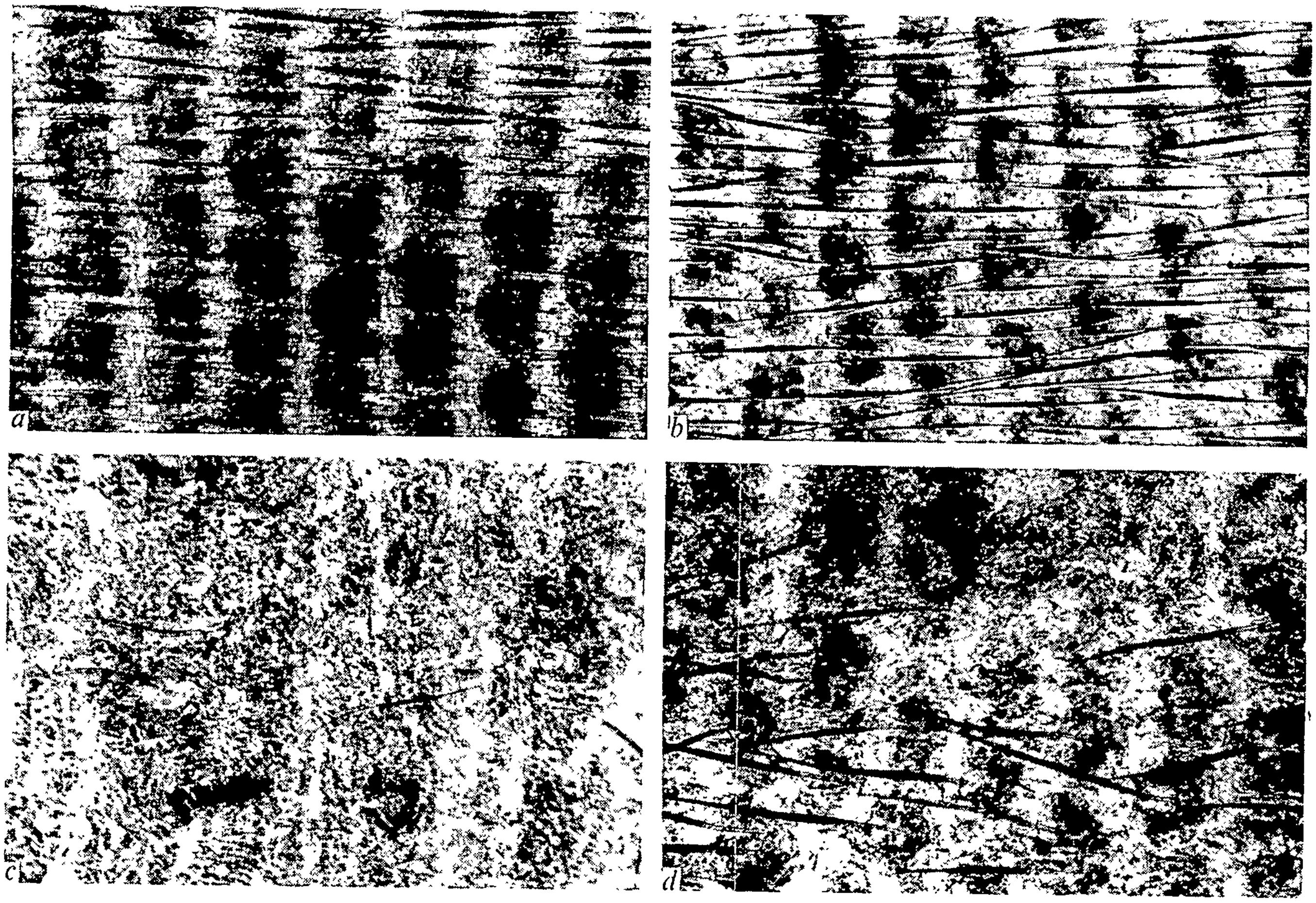

Fig. 1 Whole mounts of mouse tail skin. *a*, Normal +/+ (C57BL×C3H F_1). Regular bands of pigments and hairs. *b*, *Ta*/+ heterozygote. Less pigment, but bands regular. *c*, *Ta*/*Ta* homozygote. No regular bands, hairs sparse and abnormal. *d*, *Ta*↔+ chimaera. Patches of bald, band-free skin alternating with bands of pigment and hairs.

The tails of the chimaeras (Fig. 1*d*) differed strikingly from those of the heterozygotes. The overall banding pattern was much more irregular, and closer examination revealed a patchwork of "tabby" areas, with diffusely distributed pigment and few or no hairs, "normal" areas, with regular rows of scales showing pigment distribution and hair pattern as in homozygous normals, and in addition some "heterozygous" areas, with pigment distribution closer to that seen in heterozygotes. A statistical analysis of densitometer tracings of the tail banding patterns is in progress.

Thus the manifestation of *tabby* in aggregation chimaeras bears no simple relation to that in heterozygotes. In the gross appearance of the coat pattern, the two were very similar, though there was a tendency for chimaeras to show more of the extreme forms of manifestation. This presumably reflects the fact that tabby and normal genes are present in equal numbers in heterozygotes, but may not be equally represented in chimaeras. Marked similarity between chimaeras and heterozygotes has been reported also for coat composition and detailed hair structure in respect both of tabby[15] and of another sex-linked gene, greasy (*Gs*)[23]. In respect of all-or-none, "threshold" characters (papilla vallata, glandulae tarsales, plicae digitales), the chimaeras resembled the heterozygotes in showing some degree of intermediate or variable manifestation, but at least in the case of the plicae digitales the expression of the tabby gene was considerably stronger in the chimaeras than in the heterozygotes. A similar tendency for dominance in heterozygotes but intermediate expression in chimaeras is seen in the molars of tabby mice[16] and in some of the pleiotropic effects (for example on the xiphisternum) of the short ear gene[24]. It may indicate that dominance is due to a diffusible gene product which can operate within the cell or between neighbouring cells to allow normal development, but that in chimaeras the "patch size" is too large to allow development to be fully normalized throughout "recessive" patches. Finally, the distribution of hairs and pigment in the tail was very different in chimaeras and heterozygotes.

Much confusion has surrounded the controversy over the activity of X-linked genes in mammals. Three quite distinct questions may be posed. (1) Is the single-active-X hypothesis correct, that is, is one or other X chromosome in many mammalian XX cells randomly and irreversibly inactivated during embryonic development? There seems wide agreement that the hypothesis is essentially correct, with some reservations as to whether inactivation is total or partial, and whether it may be partially reversed in later life. The most convincing evidence of its correctness comes from studies on cloned cells from females heterozygous both for an X-linked enzyme marker and for a cytologically identifiable X chromosome[25,26]. (2) Are the orderly patterns (for example striping) seen in females heterozygous for X-linked genes consistent with the existence of two genetically distinct cell populations? The appearance of typical "heterozygous" tabby striping in the coat of $Ta/Ta \leftrightarrow +/+$ chimaeras shows that such patterns can indeed be generated by two cell populations. (3) Are the patterns clonally related to the two genetically distinct cell populations, for example are the dark and light stripes due to the activity of X^{Ta} and X^{+} chromosomes respectively? This was the assumption which Lyon originally made[1]: indeed, the existence of variegation in the coat of mice heterozygous for tabby and other X-linked genes was taken as evidence that two cell populations existed, and hence that one or other X chromosome was inactivated. It is this assumption that Grüneberg has chiefly questioned, seeking to interpret the patterns not in terms of local, autonomous gene action and clonal development ("cell heredity"), but as a manifestation of gene interaction, either within or between cells ("threshold phenomena"). In the case of the tabby coat, this question is still unresolved, but it must be remembered that the correctness of a hypothesis is in no way dependent on the correctness of the assumptions on which it was initially based. In the case of tabby tail rings, the evidence presented above makes it unlikely that the pattern seen in the heterozygote reflects the distribution of two genetically distinct cell populations. The bands of pigment are regular and of uniform width; the total amount of pigment is less than in either homozygote; hairs are distributed uniformly; no indication of a patchwork of the two homozygous phenotypes is seen. By contrast, the chimaera tails show an irregular appearance, with areas of bands similar to those seen in the homozygous normals, interrupted by areas of pigment distributed randomly, with few or no hairs, as in the homozygous tabbies, and also areas of "heterozygous" pigment distribution.

If the tails of chimaeras and heterozygotes both contain two genetically distinct cell populations clonally distributed, why do the first show the patchwork appearance expected on the basis of local gene action, while the second show an integrated pattern suggesting interaction between cells? One explanation could be that the patch size is much smaller in heterozygotes, small enough to lie within the effective range of diffusion of the hypothetical gene product. Why should the patch size be smaller in heterozygotes than in chimaeras? This may indicate either that genetically similar cells tend to remain together in chimaeras, or that X-inactivation in tail epidermis takes place relatively late in development, after the main clonal relationships have been established. It has recently been pointed out[27] that cell mobility will have a much more disruptive effect on small clones than on big ones, since the rate of expansion of a clone increases exponentially with its size, while the rate of random cell movement does not vary with the size of the clone.

Although the occurrence of X-inactivation is now widely accepted, not much information is available as to whether it occurs in every tissue of the body, and if so, at what stage of development[28,29]. In the case of retinal pigmentation, a recent study[30] has suggested that X-inactivation does not take place before 6 days *post coitum*, that is, 2 days after implantation. Further comparisons between heterozygotes for X-linked or X-translocated markers and corresponding aggregation chimaeras may throw light on these questions. Close similarity between the two, as is seen for melanocyte patterns in the coat[15], may indicate early X-inactivation, or very thorough cell mingling in the chimaeras; divergence, as in the tail epidermis, argues for later X-inactivation in the heterozygotes, or for some degree of clonal cohesion throughout development in the chimaeras.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Evolution of the Pulsar Magnetosphere

BEFORE the discovery of pulsars, Hoyle, Narlikar and Wheeler[1] reasoned that the magnetic neutron star would have a very tenuous atmosphere. In 1969, Goldreich and Julian[2] reached a different conclusion. They argued that the electromagnetic forces near the surface of a rotating magnetic neutron star are so large by comparison with the gravitational forces that charged particles must be pulled out of the star at a sufficient rate for a dense magnetosphere to be generated.

More recent work by Ruderman[3] and others[4] on the physics of the neutron star surface suggests that both conclusions are likely to be right, but at different stages in the evolution of the star. If, as now seems probable, there is a sharp boundary at the star's surface, emission of charged particles depends on the appropriate work function and temperature of the surface (thermionic emission), or alternatively on the work function and electric field (field emission). The estimates of these quantities are such that both thermionic and field emission of electrons are expected to be negligible after approximately 10^6 yr. Field emission of positive ions may be ruled out. Thermionic emission of positive ions, or evaporation of neutral atoms which may subsequently be ionized, is likely to remain large for about 10^3 yr while the surface temperature remains $\gtrsim 10^7$ K. After this time the surface temperature falls rapidly and the supply of positive ions will be greatly diminished.

These new results have an important bearing on the evolution of the pulsar magnetosphere[5]. A classification of the different stages of evolution based directly on the observational evidence has been given by Huguenin, Manchester and Taylor[6], and a theoretical classification of the different possible types of pulsar rotating field has also been worked out[7]. Here I shall interpret the observational results in the light of the theoretical results in order to obtain more insight into the evolution of the pulsar magnetosphere.

During the first 10^3 yr, the supply of both electrons and positive ions from the surface of the star is expected to be large. In this phase therefore a dense hydromagnetic magnetosphere of the type studied by Goldreich and Julian[2], Sturrock[8] and Mestel[9] is likely to be generated. It is quite probable that pulsed emission at optical or higher frequencies will occur during these first 10^3 yr, but because of the high plasma number density in the magnetosphere, observable radio pulses are much less likely. With the exception of pulsars in binary systems, no pulsars of this type with clearly identified periods have been discovered so far. (It may be that some of these pulsars have magnetospheres which are so dense that their electromagnetic fields do not even remain stationary in the rotating frame, and this would make detection of their basic periods difficult.) Pulsars in binary systems (Cen X-3, Her X-1) may receive a copious supply of plasma from their companion stars which can heat the pulsar surface by particle impact[10]. Therefore they are quite likely to have dense magnetospheres and to behave like young pulsars, in spite of the fact that their real ages are $\gg 10^3$ yr.

The Crab pulsar has an age $\sim 10^3$ yr and is therefore in a state of transition. It has already started to produce radio pulses characteristic of pulsars older than 10^3 yr, but has not yet stopped pulsing at higher frequencies. Its braking index is less than three because it still has a strongly non-vacuum magnetosphere[11]. Any estimates of its surface magnetic field strength derived from estimates of its magnetic field strength near the velocity of light cylinder[12] must be raised to allow for the expected heavy attenuation of the field by the currents in the magnetosphere.

The hydromagnetic type of magnetosphere requires a minimum continuous flow of plasma from the star. This will not be maintained after about 10^3 yr because the rate of supply of positive ions will have fallen too low. (Clearly there cannot be a continuous loss of electrons unaccompanied by positive ions, as this would result in a continuously increasing electrostatic field.) Therefore the magnetosphere must acquire non-hydromagnetic features[7], namely magnetic field lines which are pointing forwards at the velocity of light cylinder and zones where $E_{\perp} > cB$. Provided, however, that a reduced supply of positive ions is maintained, albeit at a rate much less than that required for a hydromagnetic field, $E_{\parallel}$ and charged particle drifts with respect to the rotating magnetic field lines will remain very small. Type S pulsars (simple integrated pulse profile)[6], whose ages range from about 10^4 to 10^7 yr, are therefore likely to have non-hydromagnetic magnetospheres of this type.

After approximately 10^8 yr, all particle emission from the surface of the pulsar effectively ceases, the magnetosphere becomes a high vacuum, and radio pulses are no longer generated. Before this happens, the magnetosphere must develop appreciable $E_{\parallel}$, and, more important, significant charged particle drifts with respect to the rotating magnetic field lines. (For the vacuum field these quantities are large[13].) When the charged particle drifts become significant but small, the pulsar is likely to change to Type D (drifting sub-pulse). When the drifts become large, the region from which the pulses are emitted probably becomes less well-defined, and the pulsar will then evolve to Type C (complex integrated pulse profile). Both these types are observed to occur predominantly among the older pulsars[6].

It has already been proposed by Sutton *et al.*[14] that drifting sub-pulses are caused by shearing of the plasma at the corotation break-up radius, that is, by plasma drift with respect to the rotating field. Their observational results strongly suggest that this is the case. At first sight, the fact that the sub-pulses are usually observed to drift forward through the pulse window, whereas the plasma is more likely to drift backwards with respect to the rotating field, argues against this interpretation. It is, however, quite likely that pulses emitted from the back of the emitting region will arrive at the observer before pulses emitted from the front of the region, thus producing an apparent reversal of direction of plasma drift through the region. This will happen if the azimuthal angle of pulse propagation from the back of the region is sufficiently in advance of that from the front of the region more than to compensate for the time taken for pulses to propagate across the region.

If this account of the evolution of the pulsar magnetosphere is substantially correct, then radio pulse emission mechanisms that do not involve emission of the pulses from near the velocity of light cylinder can be eliminated. According to the Sturrock radio emission mechanism[8], for instance, the pulses are emitted from near the surface of the star. Furthermore, it assumes a hydromagnetic magnetosphere, which the new results for the surface physics rule out for all the radio pulsars (apart from the Crab pulsar). The drifting sub-pulse phenomenon is very difficult to explain on the basis of emission from near the star surface or from the far field region. On the other hand, these drifting sub-pulses not only have a simple and reasonable explanation on the basis of emission from near the velocity of light cylinder, but also are observed to occur only in pulsars in the age range in which plasma drifts near the velocity of light cylinder are expected to occur.

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Faraday Rotation and Antimatter in the Universe

DATA on the Faraday rotation of polarized radio waves from extragalactic sources[1-5] have led to various interpretations[6-9]. For the general case of an ambiplasma (a plasma consisting of matter and antimatter mixed) and assuming that the plasma frequency is negligibly smaller than the wave frequency, the rate of Faraday rotation is proportional to $rB_{\parallel}\lambda^2$ (ref. 10), where r is the ambiplasma lepton residue ($r=n_e-n_{\bar{e}}$, with n_e=positron density and $n_{\bar{e}}$=electron density), $B_{\parallel}$ is the component of the magnetic field parallel to the wave vector, and λ is the wavelength. For symmetric ambiplasma, $n_{\bar{e}}=n_e$, r, and therefore the rotation rate, vanishes. I consider the consequences of this for the interpretation of the astronomical data.

The origin of the rotation is still a matter of debate, and there are three possible regions where it might take place, for example, our Galaxy, the intergalactic medium between the source and our Galaxy, and lastly the source itself. Probably rotation occurs in all three. But if I consider only sources with galactic latitude, b, such that $|b|\geq 35°$, following Fujimoto *et al.*[6], then I expect that the contribution from our Galaxy will be minimized. In addition if the magnitude of the rotation measure ρ (defined by $\Delta\theta/\lambda_0^2$, where $\Delta\theta$ is the total Faraday rotation observed, and λ_0 is the wavelength observed at the Earth) increases strongly, on average, with increasing z_s, the redshift of the source, then the chief contribution to the rotation probably occurs in the intergalactic medium, although a z_s dependence of the source contribution cannot be ruled out. The averaged magnitude of ρ does seem to increase with z_s, and I therefore consider here only the contribution from the intergalactic medium, to determine to what extent it is possible to explain the z_s dependence of the observational data on the basis of this alone. I further assume that the intergalactic magnetic field has a random structure, that is, I do not consider a homogeneous component of this field. Under this assumption a purely matter plasma in intergalactic space will cause Faraday rotations of alternating sign as the radio wave passes through regions of alternating sign of $B_{\parallel}$.

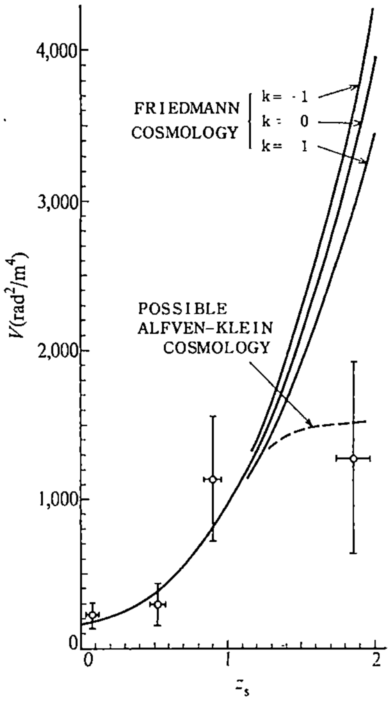

Fig. 1 The variance of the rotation measure, V (given for the observational data by the average of ρ^2 for each group of sources), as a function of the source redshift, z_s.

If the scale length of these magnetic field regions, or cells, obeys some probability law, then the polarization angle will undergo a one-dimensional Markov process similar to the random walk. The distribution of rotation measures for many sources at the same z_s should then be given by the normal distribution, and the variance of the distribution should increase with z_s. Assuming that $n_e\propto 1/l^3$ and $B\propto 1/l^2$, where l is the scale length of a cell, the variance as a function of z_s for the Friedmann cosmology (with matter only) is

$$V(z_s)=\gamma\left(\frac{2}{7}I_{7/2}+\frac{6}{5}\beta I_{5/2}+2\beta^2 I_{3/2}+2\beta^3 I_{1/2}\right) \tag{1}$$

where

$$I_a=(1+z_s-\beta)^a-(1-\beta)^a$$

$\beta=k/2$, $k=0$, 1, -1=the space curvature constant[11] and γ is a constant depending on l.

Observational values for the variance[6] give 59 sources which satisfy $|b|\geq 35°$, and I divide these into 4 groups defined by $z_s<0.3$, $z_s=0.3-0.7$, $0.7-1.1$, and $z_s>1.1$; the groups have respectively 30, 9, 12 and 8 sources. In Fig. 1 I plot the average of ρ^2 for each group, corresponding to the variance, as a function of z_s, with the average value of z_s being taken for each group. The error bars in the vertical direction are the standard errors for the sampling averages, and those in the horizontal direction represent the errors due to the scatter of the sources over z_s within the group. To compare these with equation (1) I have fitted curves (one each for $k=0$, 1 and -1) of the form $f(z_s)=V(z_s)+\chi$, with $V(z_s)$ given by equation (1), through the first three points in Fig. 1, using the method of least squares with γ and χ as fitting parameters. The resulting curves are shown in Fig. 1. For all the curves the observed value of the variance seems to be too low at $z_s=1.85$, even taking into account the considerable errors involved.

One way of explaining this is to turn to the Alfvén-Klein cosmology[12,13]. This cosmology incorporates the principle of matter–antimatter symmetry, and the situation envisaged at the present era is that there are separated cells of pure matter and pure antimatter. Provided the cells are not such that $rB_{\parallel}$ has constant sign, the combination of the matter–antimatter cells and the magnetic field cells, no matter what their respective scales are, will give rise to a Markov diffusion of the polarization angle similar to that with the magnetic field cells and matter only. So for small z_s the variance of ρ in the Alfvén–Klein cosmology will have a functional dependence on z_s given by equation (1). For large z_s, however (that is, for early times before the separation of matter and antimatter into different cells), the Alfvén–Klein cosmology envisages a state of uniformly mixed matter and antimatter, with r consequently zero; therefore $dV/dz_s=0$ for large z_s. The broken curve in Fig. 1 shows a possible $V(z_s)$ for the Alfvén–Klein cosmology.

Thus if I try to interpret the z_s dependence of ρ as being chiefly due to rotation in a random intergalactic magnetic field, the matter–antimatter symmetric cosmology offers the possibility of explaining the low variance of ρ at large z_s. But in view of the uncertainties in interpreting the Faraday rotation data, and also the small number of sources in the data groups, this evidence for the existence of antimatter in the universe, although intriguing, can hardly be regarded as conclusive.

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Endogenic Cratering Distribution on the Moon

WITHIN the cratering distribution for the Hyginus Rille floor, the chain craters represent a distribution which is distinctly different from that resulting by impact of interplanetary debris. It has been postulated[1-7] that Hyginus Rille was controlled in its development by tectonic activity along a graben zone, and some investigators[1-5,7-10] have suggested that these chain craters are volcanic in origin.

Differences in cratering densities for a lunar rille floor and its adjacent mare may have relevance to understanding the origin of some rilles[11]. High crater densities within regionally limited areas suggest that endogenic processes may supplement meteoritic processes for crater production. On Mare Cognitum[12] and the Apenninian debris surface[13] high cratering densities probably represent secondary cratering effects. On the crater floors of Ptolemaeus[14] and Copernicus[15] and the interior terrace wall units of crater Copernicus[16] cratering abundances have been attributed to igneous processes.

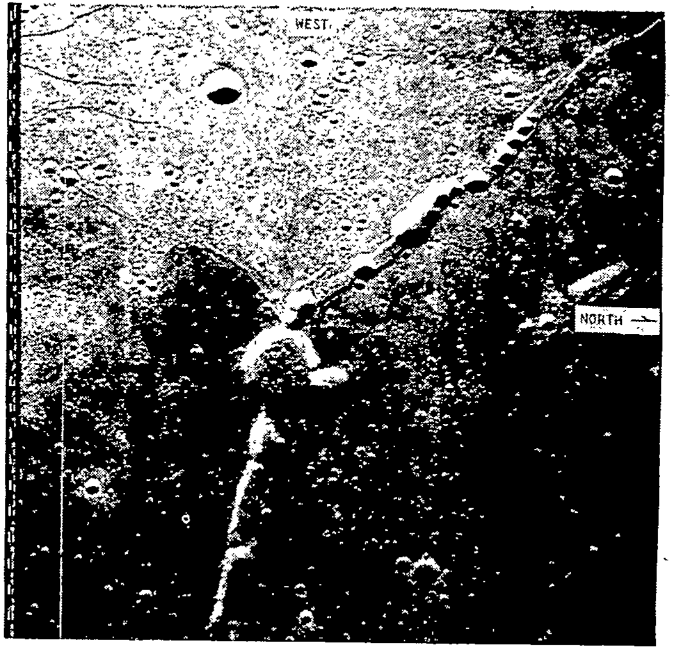

Fig. 1 A portion of Lunar Orbiter V Frame V-96M (framelets 269–246) showing the Hyginus Rille region. The largest crater, Hyginus (~10 km in diameter), is near the centre of the rille. Large low-rimmed chain craters such as the 13 in the northwest trending rille branch may have formed by endogenic mara-diatreme production processes analogous to some terrestrial craters.

Cratering densities indicate relative age relationships between surfaces. It has been suggested[9,12,13,17-20] that, in general, older surfaces display the greater crater density and include the largest craters. This age dating method assumes cratering originates chiefly by meteoritic impact.

I have made crater counts and measurements for the Hyginus Rille region from a medium resolution Lunar Orbiter V photograph (Fig. 1). Incremental and cumulative analyses of the

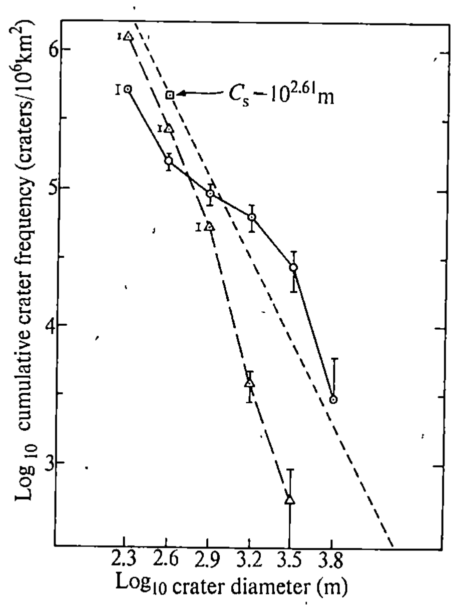

Fig. 2 Crater size-frequency distributions for the Hyginus Rille floor (⊙—⊙) and the adjacent mare (△— —△) are normalized to an area of 10^6 km². Error bars on the curves represent a ± one sigma variation. The steady-state model distribution (- - -) $N=10^{10.9}\,D^{-2}$, where crater production and destruction rates are equal, permits deriving a relative age (C_s) for a surface.

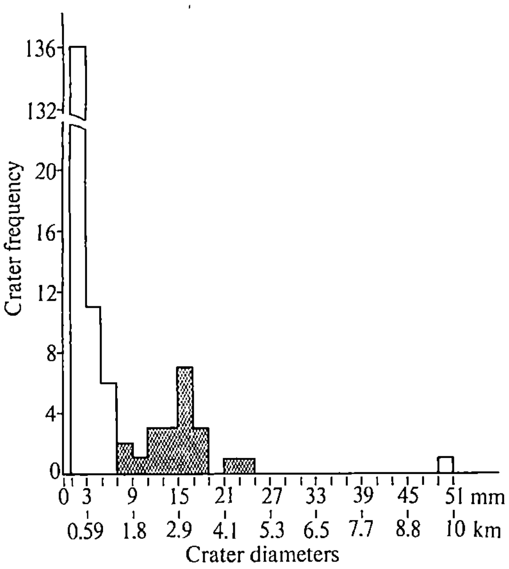

Fig. 3 Frequency of craters as a function of diameter on the Hyginus Rille floor. Shaded areas, the low-rimmed, deep-floored chain craters (these represent an endogenic size-frequency distribution which is differentiated from the predominantly meteoritic general crater distribution); white areas, smaller craters (0–51 mm).

crater-size frequency distributions show that the mare regions north and south of the rille are similar in age[21]. This adjacent mare surface has been identified as the Cayley Formation (Ica)[5].

In Fig. 2 the relative age relationships alternate: for craters ~200–540 m the rille floor appears younger, and for craters >540 m it appears older. The inference that the rille floor is older than the mare is not supported by other observational evidence. Some chain craters exhibit dark-halo deposits which subdue mare features. In the northwest rille branch 10 of 13 chain craters cross-cut the mare. Infrared observations of the eclipsed Moon show Hyginus chain craters correlate with high thermal anomalies[5,22]. These chain craters, although bouldered and fresh, cannot be Copernican age impact craters; their crater and rim morphology precludes this.

I assume a stochastic model for the formation and survival of lunar primary craters[23,24] where infilling/obliteration produces an approximate Poisson distribution. Cratering densities for the rille and mare, compared as two Poisson distributed observations, show cratering differences which are statistically significant. For diameters ~ 790 m and >1,570 m, they are significant at the 98% and 99.9% level of confidence, respectively. The cratering differences indicate endogenic processes probably control the rille cratering excess.

When the steady-state curve[26], $N=10^{10.9}\ D^{-2}$ (Fig. 2), is compared with an observed cratering distribution, $N=A\ D^{B}$, it defines two diameter-dependent distributions: a steady-state distribution where crater erasure equals crater formation, and a non-steady-state distribution, the large (L) crater "production"[19] curve, $N_L=A_L\ D^{B_L}$, where craters are produced faster than they are erased. Intersection of the steady-state and production curves determines an equilibrium crater

$$C_s = (10^{10.9}/A_L)^{1/B_L-1(-2)}$$

which is a measure of relative[17,27] age. For the adjacent mare large craters (786–6,280 m), $C_s=407\ (+60,\ -53)$ m, indicating that craters smaller than ~407 m are in steady-state. If a meteoritic origin for rille craters is assumed, then steady-state craters appear to be ≤8.7 km, but this is contrary to the evidence of the photographs. This implies that rille craters are controlled by selenological processes of non-impact origin. An Rb-Sr age ~3.65 Gy (ref. 28) and a $C_s=141$ m (ref. 27) derived for the Apollo 11 site shows that the Cayley Formation at Hyginus is older[21,29].

In Fig. 3 two rille floor cratering distributions are distinguished: a Poisson type consisting of the smaller craters, and a Gaussian which is defined in a one-to-one correspondence with 21 chain craters as an endogenic size-frequency distribution. The endogenic craters are designated the Hyginus Formation low-rimmed crater materials (CEhyl). This unit is part of a rille system volcano-tectonic complex[21] which includes the Hyginus Formation dome materials (domes, tumuli, and lava flows) and the Hyginus Formation bright deposit materials (fissure-aligned volatile/ash encrustations in subsided centres). They are late Eratosthenian or Copernican Period volcanogenic materials postdating the graben structure (Hyginus Formation, EIhy) of the rille.

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Properties of a Possible Superfluid State of ^{3}He

RECENT results by Osheroff *et al.*[1,2] on anomalies in the pressure-temperature relation and n.m.r. line of ^{3}He along the melting curve have stimulated us to consider the possibility that the much discussed[3–7] anisotropic superfluid condensation of liquid ^{3}He may in fact be occurring. Briefly these results are: first, as the volume is varied continuously in time, the curve of pressure against time exhibits a discontinuous slope at a point labelled A and a "glitch" at a point B, the slope before and after the "glitch" remaining about the same. Second, at point A the n.m.r. line starts shifting to higher frequencies until point B; it then returns to its unshifted value, but with a reduced intensity. The temperature at point A is estimated to be about 3 mK and at point B about 2 mK. If, as the nuclear resonance results show, the first anomaly is associated with the liquid, point A can be interpreted in terms of a second order phase transition in the liquid and point B, which also shows hysteresis effects, as a first order transition.

We show here that a superfluid condensation of liquid ^{3}He with a certain class of gap functions, $\Delta(\theta,\varphi)$, must be accompanied by a spin precession of finite frequency at $k=0$ due to the dipole–dipole interaction among the ^{3}He nuclei. This would show up in the resonance experiment as a shift of the experimentally measured temperature dependence and order of magnitude. We argue further that, as the temperature is decreased, a second transition may take place into a class of $\Delta(\theta,\varphi)$ for which there is no resonance shift. One such class would be one in which each spin component of the gap $\Delta^2(\theta,\varphi)$ has cubic symmetry, but preliminary analysis shows that no such state is favourable for $l=1$, and is inconclusive as yet for $l=3$. We will mention another speculation on the B state later.

The physical reason for the n.m.r. shift is that in the presence of an interaction that does not conserve spin, like the dipole–dipole interaction*, the quasiparticles are linear combinations of up and down spin particles. As the dipole–dipole interaction is a second-rank tensor, its effect will not average to zero only if the density-density correlation function for a given spin combination is of less than cubic symmetry.

We show this by considering the Hamiltonian

$$H=H_0+H_d \tag{1}$$

where H_0 includes the single particle energies, and also the interparticle interaction $V(r,r')$ which, if attractive in the lth particle wave, leads to superfluidity with an order parameter whose $\alpha\beta$ component in the spin space is

$$\Delta_l^{\alpha\beta}(\mathbf{r}-\mathbf{r}')=V_l(\mathbf{r},\mathbf{r}')\langle\Psi_\alpha(\mathbf{r})\Psi_\beta(\mathbf{r}')\rangle \tag{2}$$

In equation (2), $\Psi_\alpha(r)$ are the field operators for the αth z component of spin. H_d is the dipole–dipole interaction, which may be written as

$$H_d=\sum_{\alpha\beta\nu\delta}\int d\mathbf{r}\int d\mathbf{r}'\, W_{\alpha\beta}^{\nu\delta}(\mathbf{r}-\mathbf{r}')\Psi_\delta^+(\mathbf{r})\Psi_\nu^+(\mathbf{r}')\Psi_\beta(\mathbf{r}')\Psi_\alpha(\mathbf{r}) \tag{3}$$

We now write equations of motion for $\Psi_\alpha(r)$, $\Psi_\alpha^+(r)$ and linearize them by the Bogolubov method to obtain

$$i\hbar\dot{\Psi}_\alpha(\mathbf{r})=h(\mathbf{r})\Psi_\alpha(\mathbf{r})+\sum_\beta{}'\int d\mathbf{r}'\, V_l(\mathbf{r}-\mathbf{r}')\langle\Psi_\alpha(\mathbf{r})\Psi_\beta(\mathbf{r}')\rangle\Psi_\beta^+(\mathbf{r}')+$$
$$\sum_{\beta\nu\delta}{}'\int d\mathbf{r}'\, W_{\nu\delta}^{\alpha\beta}(\mathbf{r}-\mathbf{r}')\langle\Psi_\nu(\mathbf{r})\Psi_\delta(\mathbf{r}')\rangle\Psi_\beta^+(\mathbf{r}') \tag{4}$$

and similarly an equation for $\Psi_\alpha^+(r)$, where the prime over the sum indicates that the states in $\langle\ \ \rangle$ must be taken to be singlet for even values of l and triplet for odd values of l. On using now the fact that $\langle\Psi_\nu(r)\Psi_\delta(r')\rangle=-\langle\Psi_\nu(r)\Psi_\delta(r')\rangle$ for even values of l (singlet states), it is seen that the last term in equation (4) adds up to zero. We may thus confine our attention to triplet spin state pairing.

In the standard fashion, we now use the transformation

$$\Psi_\alpha(\mathbf{r})=\sum_{\mathbf{k}}u_{\mathbf{k}\alpha}\, e^{i\mathbf{k}.\mathbf{r}}\, \mathrm{v}_{\mathbf{k}\alpha}+\nu_{\mathbf{k}\alpha}\, e^{-i\mathbf{k}.\mathbf{r}}\, \mathrm{v}_{\mathbf{k}\alpha}^+ \tag{5}$$

and require that

$$[H,\mathrm{v}_{\mathbf{k}\alpha}]=-E\mathrm{v}_{\mathbf{k}\alpha},\text{ and so on} \tag{6}$$

to obtain

$$Eu_{\mathbf{k}\alpha}\simeq\varepsilon_{\mathbf{k}}u_{\mathbf{k}\alpha}+\sum_\beta\Delta^{\alpha\beta}(\mathbf{k})\nu_{\mathbf{k}\beta}+\sum_{\upsilon\Delta\beta}D_{\mu\nu}^{\alpha\beta}(\mathbf{k})\nu_{\mathbf{k}\beta} \tag{7}$$

and similar equations for $\nu_{k\alpha}$. In equation (7) $\Delta^{\alpha\beta}(\mathbf{k})$ is the Fourier transform of $\Delta_{\nu\delta}^{\alpha\beta}(\mathbf{r}-\mathbf{r}')$ and $D^{\alpha\beta}$ the Fourier transform

$$\mathrm{D}_{\nu\delta}^{\alpha\beta}(r)=W_{\nu\delta}^{\alpha\beta}(\mathbf{r})\langle\Psi_\nu(\mathrm{o})\Psi_\delta(\mathbf{r})\rangle \tag{8}$$

Next, we diagonalize the set of equations (7) and make the approximation that $D(\mathbf{k})\ll\Delta(\mathbf{k})$ to obtain

$$E^2\simeq\varepsilon_{\mathbf{k}}^2+\Delta_{\mathbf{k}}^2\pm|\Delta_{\mathbf{k}}^{\uparrow\uparrow}\mathrm{d}_{\mathbf{k}}^{\downarrow\uparrow *}+\Delta_{\mathbf{k}}^{\uparrow\downarrow}d_{\mathbf{k}}^{\downarrow\downarrow *}+\Delta_{\mathbf{k}}^{\downarrow\uparrow *}d_{\mathbf{k}}^{\uparrow\uparrow}+\Delta_{\mathbf{k}}^{\downarrow\downarrow *}d_{\mathbf{k}}^{\uparrow\downarrow}| \tag{9}$$

where

$$d_{\mathbf{k}}^{\alpha\beta}=\sum_{\nu\delta}D_{\nu\delta}^{\alpha\beta}(\mathbf{k})$$

In deriving equation (9), it has been assumed that $\Delta(\mathbf{k})$ is unitary. If $\Delta(\mathbf{k})$ is not unitary a spontaneous breaking of spin degeneracy is implied; we have not yet investigated the resulting n.m.r. behaviour for this case, which may well be the ground state for all odd $l\gtrsim3$.

The lifting of the spin degeneracy represented by equation (10) shows up in the n.m.r. signal as an average shift from the frequency $\omega_0=\gamma H$ to ω given by

$$\omega^2-\omega_0^2\simeq2\Sigma|\Delta_{\mathbf{k}}^{\uparrow\uparrow}\,\mathrm{d}_{\mathbf{k}}^{\downarrow\uparrow}{}^*+\Delta_{\mathbf{k}}^{\uparrow\downarrow}d_{\mathbf{k}}^{\downarrow\downarrow}{}^*+\Delta_{\mathbf{k}}^{\downarrow\uparrow}{}^*d_{\mathbf{k}}^{\uparrow\uparrow}+\Delta_{\mathbf{k}}^{\downarrow\downarrow}{}^*d_{\mathbf{k}}^{\uparrow\downarrow}| \tag{10}$$

From equation (10) it is evident that because $W(\mathbf{k})$ is a traceless, symmetric second rank tensor, $\omega^2-\omega_0^2$ is non-zero only if one component $|\langle C_{\mathbf{k}\alpha}C_{-\mathbf{k}\beta}\rangle|^2(\equiv P_{\mathbf{k}}^{\alpha\beta})$ is of lower than cubic symmetry. The observation of an n.m.r. shift would thus indicate such a paired state.

It is also seen that equation (10) is proportional to the square of the number of condensed pairs and hence to T_C-T for T just below T_C. On using a dipole–dipole interaction of 1 gauss and estimating the other parameters from the Fermi energy of about 1 K, and the experimentally observed T_C of about 3 mK, we obtain

$$\omega^2-\omega_0^2\simeq10^{10}\left(\frac{T_C-T}{T_C}\right)(c/s)^2$$

which has the right temperature dependence and the correct order of magnitude.

Now we discuss what angular momentum component the pairing may be in. The $l=1$ state does give the right order of n.m.r. shift. The correct $l=1$ state as derived by Balian and Werthamer[7] is, however, one which gives the lowest free energy for all temperatures, and thus the B transition would be hard to understand on this basis. Further, it would give an n.m.r. shift at all temperatures.

Unfortunately the case for $l=3$ has not been worked out; similar things may in principle go on there. Our preliminary investigation shows, however, that with a unitary $\Delta(\mathbf{k})$ the "cubic" states that can be constructed from $l=3$ are not favourable. For $\Delta(\mathbf{k})$ not unitary, however, it is possible that "cubic" states of low enough free energy can be constructed to give the B phase. These would not have an n.m.r. shift using the mechanism discussed above and may have a sharply lower magnetic susceptibility than "unitary" states; however, we do not yet understand their other properties. Another possibility to account for the B transition is that the attraction parameter for $l=2$ is smaller than that for $l=3$ by less than 10%. As the free energy for $l=2$ drops faster than for $l=3$, this can account for all the features of the B transition—its first order nature, the disappearance of the n.m.r. shift, the decrease in the susceptibility, and so on. We doubt that values of l higher than 3 are involved, because the interaction parameter must fall off with increasing l. Earlier calculations[3] showed $l=2$ to be the most promising. We suspect that $l=3$ wins because of exchange enhancement.

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* We note that there may be a second spin non-conserving interaction of very roughly the same order of magnitude: the atomic-orbit-nuclear spin interaction. This interaction is of order 100 oersted for H_2 and may here be of the order of 1% of that number for two atoms in contact. It will be interesting when the experiments are better understood quantitatively to look for effects of such an **L·I** interaction. This interaction is discussed in, for example, ref. 8.

We now speculate on the static susceptibility as deduced from the strength of the n.m.r. absorption. In the "axial" state the susceptibility will in general be a tensor, and in an external magnetic field we expect the spins to be lined up to give the maximum susceptibility, just as, for example, in an antiferromagnet. The coercive field (~30 gauss) experimentally required before any n.m.r. shift is observed is $\simeq \sqrt{H_d\Delta}$, very reminiscent of a spin flip transition in an antiferromagnet. We suspect that the strength of the n.m.r. absorption reflects the perpendicular susceptibility, which we expect to be nearly temperature independent if the state is like the equal spin pairing state that Anderson and Morel[6] investigated for $l=1$. One possible way to test for such a state is to vary the angle of the polarization of the r.f. field in the n.m.r. experiment with respect to the d.c. field. On the other hand, in a "cubic" phase, the susceptibility tensor will be isotropic; hence, we might expect a drop in the susceptibility at B. The magnitude of the drop may crucially depend on the fact that if χ_0, the "single particle" susceptibility, drops, then χ, the "many body" susceptibility, drops even more.

As there is a situation of broken symmetry, one would expect in general to have domains formed. The field of 30 gauss probably aligns the domains. The non-equilibrium effects reported by Osheroff *et al.* may be associated with domains.

The behaviour of dP/dt at A reported by Osheroff *et al.*[1] is understood if the jump in the specific heat at T_C is about a factor of two and we assume that the solid is not in thermal contact with the liquid. This is the right magnitude for the jump in the specific heat for the $l=3$ transition.

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Subduction and Aseismic Ridges

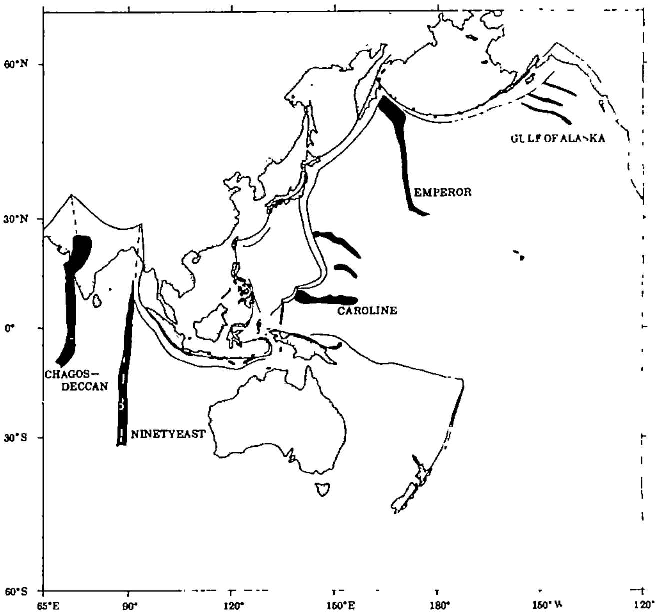

Fig. 1 Simplified sketches of major aseismic ridges and seamount chains near island arcs of the Pacific and Indian oceans, based on standard bathymetric charts and the new north Pacific atlas[8]. Plate collision boundaries shown by single or double lines, the latter showing both volcanic arc and trench. Marcus–Necker Ridge intersects the northern Marianas arc between the Emperor and Caroline ridges. The Deccan Traps are considered part of Chagos–Deccan volcanic line[9].

WHETHER or not aseismic ridges and seamounts on the ocean floor are due to stationary hot spots[1-7] or some other process, one may ask what happens when an aseismic ridge is forced into a subduction zone. Here I consider one aspect of the problem, namely whether or not the plan view of island arcs and their associated trenches has been influenced by aseismic ridges being subducted. Island arc type subduction occurs primarily in the western Pacific and the Indian Oceans. As indicated in Fig. 1, there are a small number of aseismic ridges in the vicinity of the north and western Pacific and Indian trenches. The bathymetric charts recently published by Chase *et al.*[8] were used to obtain the general outlines of the Pacific aseismic ridges. The two most massive Pacific ridges, the Emperor and Caroline, intersect the trench system near prominent cusps, where one arc gives way to the next. In addition, the Marcus–Necker ridge intersects the northern edge of the arcuate portion of the Marianas trench; the Gulf of Alaska seamounts, presumably generated by the Juan de Fuca and/or its neighbour, the Yellowstone plume[5-7], intersect the Aleutians only slightly west of the cuspate eastern end of the Aleutian arc. In the Indian Ocean, the two principal cusps in the boundary between Asian and Indo-Australian plates are now intra-continental. It may reasonably be supposed, from its arcuate character and continuity with the Indonesian arc, that the Himalayan arc replicates the shape of an extinct island arc system lying in the Tethyan Ocean, that lay between India and central Asia until it was closed by subduction in later Tertiary times. Whether or not the Himalayan arc preserves the shape of an old island arc, the Indian Ocean's two prominent aseismic ridges[9] extend, with comparatively minor extrapolation, into the two major cusps of the Himalayan tectonic arc.

The number of examples are small—a typical predicament for observations involving features of continental dimensions. But it seems unlikely to me that the coincidence of cusps with aseismic ridges is mere chance. Therefore, I suggest the qualitative model of Fig. 2. Inner arc spreading, probably episodic, causes the volcanic arc to migrate away from the continent[10-12], while oceanic crust, carrying aseismic ridges as passive cargo, is subducted according to the now-conventional model. When a massive segment of an aseismic ridge enters the trench, however, inner arc spreading is slowed by the positive buoyancy of the volcanic pile, which resists subduction. The subduction boundary thus acquires a cusp; a number of such cusps produces a series of arcs. Because plumes or hot spots start, fluctuate in discharge[13] and presumably die, there is no necessity that a cusp must have a massive aseismic ridge going into it at present. Even if aseismic ridges did not thicken and thin, there is no reason why a ridge should parallel the vector of relative motion between island arc and oceanic plate: if it is not exactly parallel, the present intersection of island arc with aseismic ridge may be displaced from where it was when the cusp was created (Fig. 2). Conversely, however, the hypothesis demands that where a massive aseismic ridge intersects an island arc system, there should be a cusp; the data of Fig. 1 suggest that this is so. In the case of the Pacific

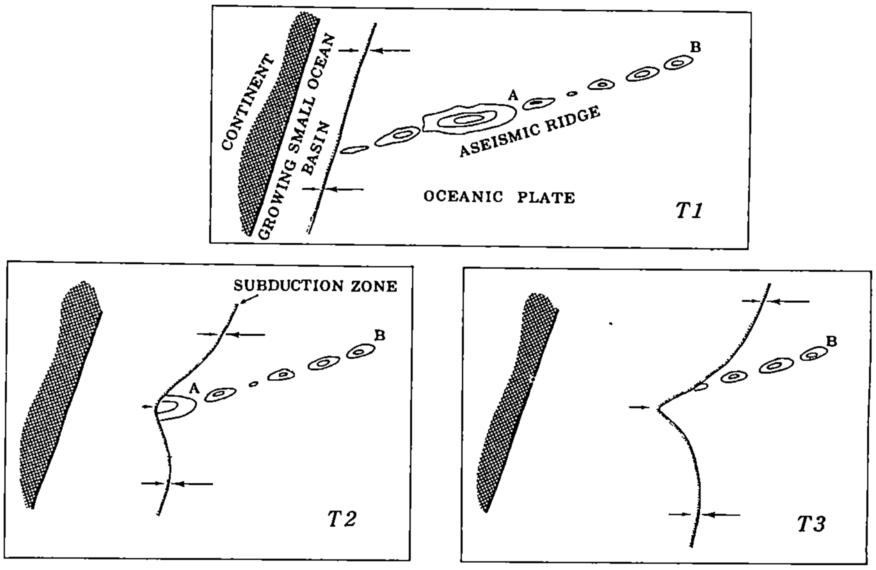

Fig. 2 Diagrammatic explanation for coincidence between aseismic ridges and island arc cusps. Owing to buoyancy of lithosphere containing massive, relatively low density segment of aseismic ridge, inner arc spreading is slowed. An aseismic ridge will not, in general, parallel the subduction vector. Chronological sequence T1→T2→T3.

arcs, the kinetics of late Tertiary plate motion has been such[14] that aseismic ridges are nearly parallel the vectors of relative motion. Were this not the case, the juxtaposition of cusps and ridges would only hold for the very recent geological past, and the cusps and arcs would have had to acquire their shape very recently for the hypothesis to hold. The Marianas arc acquired its present shape since the Pliocene[10–12]: there has thus been little opportunity for the aseismic ridges to move away from the cusps. Exactly when the other arcs acquired their present curvature is still unknown.

In the case of the Chagos–Deccan and Ninety East aseismic ridges the hypothesis (Fig. 2) demands that northward extensions of these hot spot trails existed in the now-closed Tethys, and that the Indo–Australian plate has moved essentially due north since the time their extensions were subducted. The assumption of such persistent northward motion finds strong support in palaeomagnetic[15] and plate tectonic[16] evidence, but the hot spot/plume concept[1–7] uses the aseismic ridges themselves as convincing evidence. If Asia is taken to be nearly fixed with respect to the mantle, to first order, the Ninety East and Chagos–Deccan aseismic ridges record not only the motion between the Indo–Australian plate and the mantle, but also the motion between this plate and Asia. The Chagos–Deccan lineament shows that northward motion has continued from about 60–65 m.y. BP, the age of the Deccan Traps[15], to later Tertiary times. Only the southern to central parts of the Ninety East Ridge are as young as the Deccan Traps; the northern surviving limit is Campanian or older[17]. So it seems that the aseismic ridges have roughly paralleled the relative plate motion vectors at the cusps of the Himalayan arc for at least 80 m.y. It can therefore not be argued that the location of the cusps on the extensions of the two aseismic ridges is an accidental arrangement of recent geological time, postdating the formation of the arcs.

The hypothesis that aseismic ridges inhibit inner arc spreading (Fig. 2) depends on whether or not the ridges have enough positive buoyancy.

The more massive ridges have widths of ~50 to 500 km; the excess crustal thickness is generally supposed to be in the form of basalts and intrusives of basaltic composition deposited on pre-existing oceanic crust. In the case of the aseismic ridge produced by the Iceland plume, crustal thickness varies from about 8–15 km on Iceland[18] to 15–20 km near the Faeroes Islands[19]. The Hawaiian ridge generally rises 3 to 10 km above the average top of the oceanic crust. At three relatively massive portions of the ridge—Hawaii, Oahu, and Gardner Pinnacles—geophysical data indicate that the crust is thickened about 10 km, of which 2 km is attributed to subsidence and 8 km to transformed upper mantle[20]. Detailed refraction measurements in the south of Hawaii—close to the present plume position—showed crustal thickness varying from 12 to 17 km (ref. 21). In summary, the normal oceanic crust is augmented by about 10 km basaltic crust, of average density no more than 3.0–3.1 gm cm^{-3}, in the more massive portions of aseismic ridges. If the subcrustal portion of the lithospheric plate has a density 3.3 gm cm^{-3}, the average total lithospheric density is decreased by 0.02 to 0.03 gm cm^{-3} for aseismic ridge densities of 3.0 to 3.1 gm cm^{-3}. For an upper mantle density of 3.4 gm cm^{-3} the density decreases are 0.03 to 0.05 gm cm^{-3}. At present the process of subduction and inner arc spreading are not understood sufficiently well to decide whether density differences of this order are significant. But the differences could locally overcome the negative buoyancy of the colder subducted slab, which is held to be a partial driving force for sea floor spreading[22]. The models calculated by Minear and Toksöz[23] show that for subduction velocities near 1 cm yr^{-1}, a zone interior to the downthrust slab and extending from about 100 km to 300 km in depth is 0.01 gm cm^{-3} denser than the surrounding mantle. For a subduction speed of 8 cm yr^{-1}, an 80 km thick interior zone extending from depths of 80 to 500 km is about 0.04 gm cm^{-3} denser. These density excesses are similar in magnitude to average-density deficits of 0.02 to 0.05 gm cm^{-3} due to a 10 km thick aseismic ridge riding on a normal oceanic plate. The density excess applies to the whole downgoing plate, whereas the aseismic ridge is only 50 to 500 km wide; however, broader density anomalies of the subcrustal hot spot lithosphere cannot be ruled out.

As far as previous explanations for the curvature of island arcs are concerned, relatively few students of subduction zones seem to have considered this problem. An example of a pre-seafloor spreading explanation is Lake's suggestion[24,25] that plane fractures intersecting a spherical Earth would produce circular arcs on the surface. A more recent argument[26] is based on the proof that a flexible, inextensible, thin spherical shell may be bent inwards through an angle θ only on a circle whose radius of curvature is $1/2\ \theta$. The data supporting this are: the downthrust lithospheric slab, thin compared to the radius of the Earth, typically dips 45° into the mantle; and island arc curvature radii—expressed in angular measure on the sphere—are typically one half this value. But the Tonga–Kermadec "island arc" and the subduction zones on the west coast of south and central America are either straight or concave seaward. The Marianas arc has acquired its curvature in later Tertiary times[10–12]; its ancestor, the Palau–Kyushu Ridge, was essentially straight. It follows that the curvature of the island arcs evolved gradually, and the bent sphere model[26] is unrealistic. There may nevertheless be a minimum-energy consideration that tends to make straight "arcs" evolve into curved ones. Even if this is so, some irregularity is needed to make cusps form at one point rather than another, and aseismic ridges may serve in exactly that capacity. Major fractures in the oceanic crust might be proposed as another such irregularity; however, none of the definite examples of fracture zones being subducted under island arcs seem to have influenced the curvature of the arcs.

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A Topographic Interpretation of the Mathematician Ridge, Clipperton Ridge, East Pacific Rise System

Within the framework of plate tectonics, dating of the ocean floor has been almost exclusively achieved by studies of magnetic anomalies. But a north–south striking mid-ocean ridge system generating new seafloor in the equatorial region produces magnetic anomalies which are of small amplitude and are frequently distorted and disguised by magnetic "noise". The correspondence between the absolute depth of oceanic crust and its age[1] has provided an alternative method of age dating the oceanic crust anywhere in the world's oceans, provided, of course, that the crust was generated by a seafloor spreading system. Such a correlation tool has been used on the East Pacific Rise (Fig. 1) between 20° N and the equator[1] and between 0° and 20° S (ref. 2).

This method assumes that the lithospheric plate is isostatically compensated. All elevation is thus caused by thermal expansion as new hot crust is added to the plate at the ridge crest and thermal contraction as the newly solidified crust spreads from the ridge axis and cools. A remarkable correspondence of age to depth was found in the Pacific, Atlantic, and Indian Oceans[1].

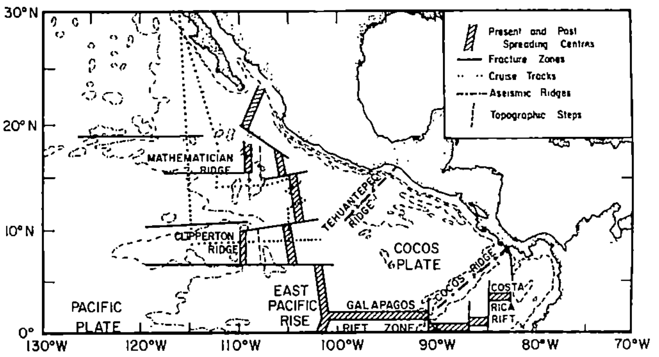

Fig. 1 Physiographic diagram of the central eastern Pacific. The light dot-dash line is the 4,000 m contour.

Sclater *et al.*[1] presented a tectonic interpretation of the East Pacific Rise system north of the equator based upon this age–depth relation. They found that the East Pacific Rise is a relatively young feature, the seafloor spreading centre having jumped from a fossil ridge crest to the west of the present axis approximately 4 m.y. BP. The boundary between the fossil system, the Mathematician Ridge, and the East Pacific Rise is marked by a distinct topographic step caused by an age discontinuity across the step. They described the Mathematician Ridge as an approximately north–south ridge extending from 18° N to 12° N having an average crestal depth of 3,200 m and smoothly deepening slopes characteristic of a mid-ocean ridge system. They also postulated the existence of another fossil ridge, the Clipperton Ridge, striking north–south from 10° N to 8° N. Herron[3], using magnetic anomalies to interpret crestal age, found anomaly 5 symmetrically distributed about the East Pacific Rise at 14° N. She thus concluded that magnetic data do not agree with the topographic age of the axial shift, but rather support a radical shift in the position of the axis between 10 and 15 m.y. BP.

Anderson and Sclater[2] used the depth/age method to interpret the tectonics of the East Pacific Rise from the equator to 20° S. They found a similar fossil ridge called the Galapagos Rise, on the Nazca Plate, and postulated that a jump in the spreading centre had occurred ~6 m.y. BP to the present East Pacific Rise system. Herron[3], again using magnetic anomalies, found that the Galapagos Rise had jumped 10 m.y. BP.

Sclater *et al.*[1] used the north Pacific to construct their topography/age curve by correlating crestal depth with the well-known magnetic structure from Atwater and Menard[4]. The depth–age relationship is thus based upon magnetic anomalies. It is therefore extremely disturbing to find the seeming disagreement between the two methods in the age of the axial jump in the eastern Pacific.

In an attempt to shed light upon the solution to this problem, two long east–west topographic and magnetic lines were run across the Clipperton Ridge–East Pacific Rise at 8° N and the Mathematician Ridge–East Pacific Rise at 14° N on RV Thomas Thompson cruise TT-65 in November 1971. The results of these lines clearly show the compatibility between the magnetic and topographic interpretations of the Mathematician Ridge, Clipperton Ridge, and East Pacific Rise system.

A jump in spreading centre is essentially a perturbation of the plate tectonic model. The dependence of depth on age away from spreading centres theoretically requires that such a jump produce a step or ramp in the topography of the ridge[2]. The depth of the top of the step should correspond to the depth of the crest of the fossil ridge, because both are the same age, and the depth of the bottom of the step should correspond to the age of crust into which the new spreading centre jumped. The observation of such steps on the flanks of the East Pacific Rise indicates that the lithospheric plate model's assumptions of vertical cooling and intrusion are valid on the East Pacific Rise system.

The profile across the Clipperton Ridge–East Pacific Rise at 8° N shows a clear step in the topography between the two ridges (Fig. 2). Papagayo I profile from Scripps Institution of Oceanography at 9° N substantiates this interpretation. The depth of the East Pacific Rise crest is 2,700 m. The depth of the Clipperton Ridge crest and the top of the step is 3,500 m, a depth corresponding to an age of 7.5 m.y. (ref. 1). The depth of the bottom of the jump is 3,750 m corresponding to an age of 12 m.y. BP. The magnetics are uninterpretable except for the central anomaly on the East Pacific Rise crest. Thus the spreading centre jumped from the Clipperton Ridge 220 km to the east at 7.5 m.y. BP to begin spreading in 4.5 m.y. old crust.

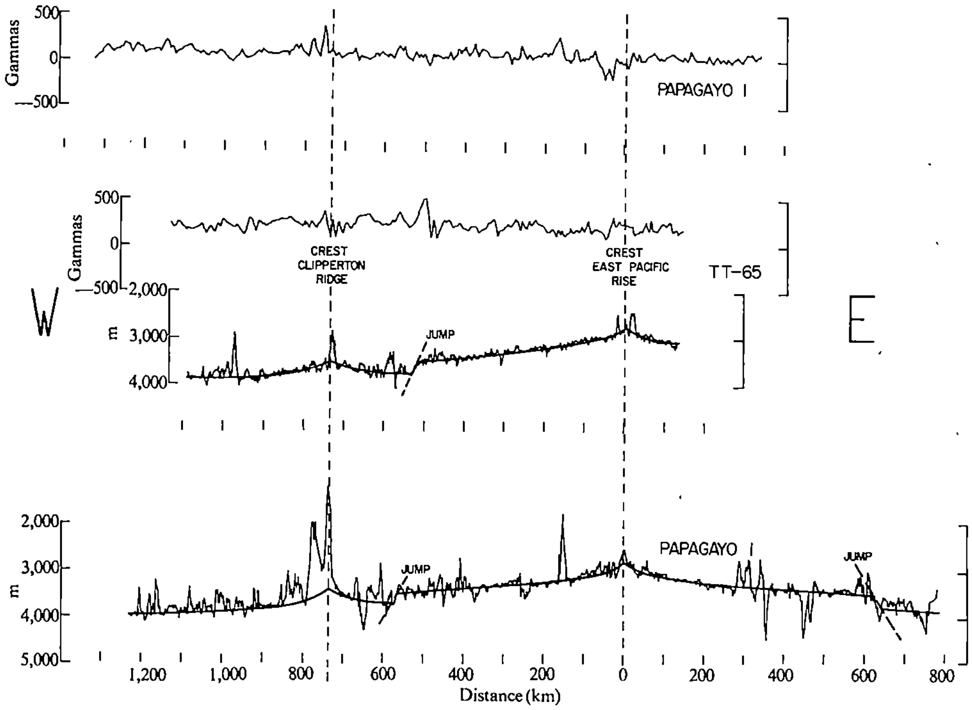

Fig. 2 East–west bathymetric and magnetic profiles at 8° N (TT-65) and 9° N (Papagayo I) across the Clipperton Ridge and East Pacific Rise. The solid line is the best fitting topographic curve through the data.

Spreading rates can be determined from the slope of the topographic profile and have been demonstrated to be accurate to $\pm 10\%$ by Anderson and Sclater[2]. The 8° N profile indicates that the East Pacific Rise is spreading at 6.5 cm^{-1} yr half-rate, and the Clipperton Ridge was spreading at 4.0 cm yr^{-1} half-rate before the jump.

The profile between the Mathematician Ridge and East Pacific Rise at 14° N shows extremely rough topography across the Mathematician Ridge but no topographic step or smooth slope away from the crest. Rather, the crust to the west of the Mathematician Ridge has the proper depth to be generated from the East Pacific Rise. In other words, there is no indication that the rough topography is a fossil spreading centre and no evidence that a jump has occurred at 14° N. Further, the magnetic anomalies are identifiable through anomaly 5 and indicate a spreading rate of 4.6 cm yr^{-1} half-rate.

Sclater *et al.*[1] show that the Mathematician Ridge at 16° N has smooth, continuously deepening slopes. To examine further the clear difference in physiography between the seamounts at 14° N and the ridge at 16° N, we ran a north–south seismic reflexion profile on the flanks of both features from 18° N to 14° N (Fig. 3). The topography drops from an unsedimented shallow northern section which is the flank of the fossil spreading centre to the well-sedimented flanks of the seamount province. This step occurs at 15° 15′ N. Ages across this step jump from the 4.5 m.y. old crust of the fossil ridge to 12 m.y. old crust generated originally on the East Pacific Rise.

Thus, Herron[3] found anomaly 5 associated with a section of the East Pacific Rise which did not jump when the Clipperton Ridge centre jumped 7.5 m.y. BP to the present East Pacific Rise or when the Mathematician Ridge jumped to the present system 4 m.y. BP.

The Mathematician Ridge system extends only from 18° N to 15° 15′ N, and its termination corresponds to a dramatic "kink" in the 4,000 m contour toward the East Pacific Rise crest at this latitude (Fig. 1).

The disagreement between topographic and magnetic interpretations of the East Pacific Rise system north of the equator is thus totally resolved. Further, this adjustment in the Mathematician Ridge system gives an even better fit of the Cainozoic reconstruction of the East Pacific Rise presented in Sclater *et al.* (ref. 1, Fig. 14) to the observed topography.

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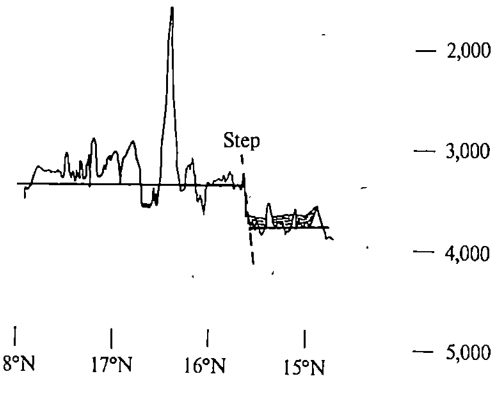

Fig. 3 North–south seismic reflexion profile run along 112° W longitude. Generally <20 m of sediment exists north of the step, and up to 125 m is found to the south. Solid line is best-fitting topographic line through data.

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Infrared Magnetic Circular Dichroism in the Study of Metalloproteins

Magnetic circular dichroism (MCD) is the differential absorption of left and right circularly polarized light induced by a magnetic field[1–4]. By contrast with natural circular dichroism (CD), MCD is a property of all materials. Until now no instrumentation has been available for measuring CD and MCD in the near infrared (IR) spectral region with the high sensitivity routine in the visible and near ultraviolet. Some CD studies at wavelengths greater than 1 μm have been made on iron-sulphur proteins[5,6]. No MCD measurements have been made in this region. The recent development of photoelastic modulators (PEM)[7] has made this possible and at the University of Southern California we have built a near IR CD and MCD instrument incorporating an 'infrasil' quartz PEM[8]. The instrument has a sensitivity of close to 10^{-5} absorbance units over its spectral range of 800–3,000 nm and employs magnetic fields up to 60 kgauss. We believe this will permit important new studies of metalloproteins and here report initial results on haemoproteins.

Most molecules of biological interest exhibit no electronic absorption, and hence no CD or MCD, in the near IR. However, in proteins containing transition-metal ions electronic absorption bands commonly occur in the near IR. The study of these bands is often useful in elucidating metal-ligand stereochemistry and electronic structure (refs. 5, 6, 9, 10 and Makinen and Eaton, unpublished work). Almost all haemoproteins exhibit near IR absorption bands and, of the entire electronic spectrum, these are the most sensitive to metal coordination, oxidation state and spin state[10,11]. The near IR bands of ferric derivatives have recently been used by Perutz *et al.*[12,13] to investigate haem-haem interaction in ligand binding by mixed-oxidation-state haemoglobins. The assignment of these bands is necessary for the detailed interrelation of spectra and structure. Assignments have previously been suggested for the ferric spectra[11,14] but not firmly established. We have made CD and MCD measurements on two high-spin ferric compounds [acid methaemoglobin (metHb) and acid metmyoglobin (metMb)] and two low-spin ferric derivatives [cyanomethaemoglobin (metHbCN) and cyanometmyoglobin (metMbCN)]. The MCD of the low-spin near IR bands provides definite evidence in favour of a porphyrin-to-iron charge-transfer mechanism for these transitions. The shape of the MCD is quite different for the high-spin bands and MCD should therefore be a much more diagnostic tool than absorption spectroscopy for studying spin-state equilibria in ferric haemoproteins.

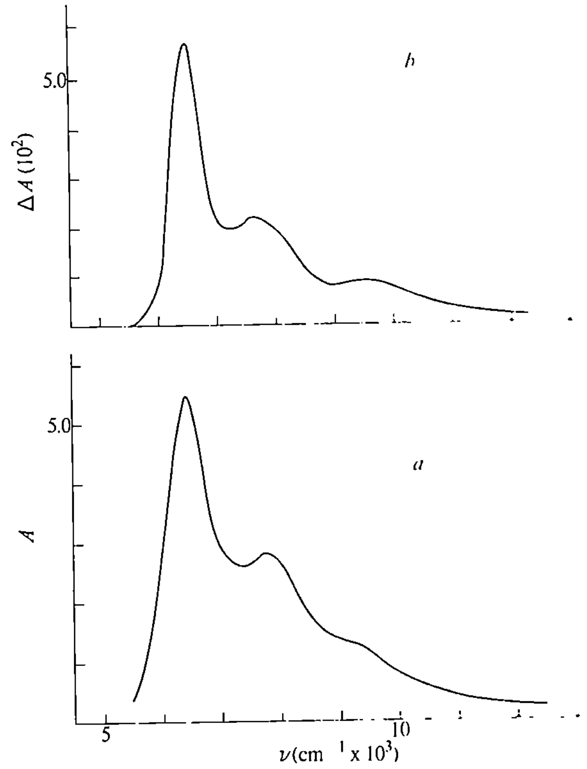

Fig. 1 Near infrared MCD and absorption of human cyanomethaemoglobin in D_2O (1.0 cm pathlength, 0.0013 M in haem, 0.1 M potassium phosphate buffer, pH=6.6, room temperature). Oxyhaemoglobin, prepared according to Perutz[17], was oxidized with excess potassium ferricyanide, passed through a 'Sephadex G-25' column, and dialysed against a 0.1 M potassium phosphate buffer in D_2O for three days. The cyanide complex was formed by the addition of excess solid potassium cyanide. *a*, Absorption spectrum measured with a 'Cary 14' spectrophotometer. Reference is 1 cm path of dialysate. *b*, MCD at $H = +39.2$ kG. $\Delta A \equiv A_L - A_R$, where L and R denote left and right circular polarizations, respectively, and A is absorbance. Spectral bandwidth is ~4 nm, and time constant 3 s.

The absorption spectrum of a room-temperature solution of human metHbCN in the region 800 2,000 nm (12,500–5,000 cm^{-1}) is shown in Fig. 1*a*. The spectrum of sperm-whale metMbCN is very similar. We have measured the CD and MCD of these solutions at room temperature in the region 800–2,000 nm, the latter with magnetic fields up to 50 kG. Typical spectral bandwidths and time constants of ~4 nm and 3 s provide a CD sensitivity close to 10^{-5} absorbance units. Without magnetic fields we observe no CD due to the IR transitions. On the other hand a large MCD is observed, as shown in Fig. 1*b* for metHbCN. The MCD of metMbCN is very similar.

To interpret the spectra we use a molecular orbital model. The highest occupied orbitals are nearly three-fold degenerate iron d orbitals, belonging to t_{2g} and b_{2g}, e_g in O_h and D_{4h} symmetries respectively. In the ferric, low-spin cyanide derivatives, five electrons occupy these orbitals in the lowest electronic configuration and lead to three close-lying Kramers doublets whose spacing and wave-functions depend sensitively on the d orbital splittings and spin-orbit coupling. Porphyrin π-electron theory[15] predicts the highest filled orbitals to be two, nearly-degenerate orbitals belonging to a_{1u} and a_{2u} in D_{4h} symmetry. Excitations from these orbitals into the d shell hole lead to two charge-transfer states, $^2A_{1u}$ and $^2A_{2u}$ in D_{4h} symmetry, transitions to which are fully allowed. In the porphyrin-to-iron assignment, the near IR bands are thus attributed to these two, nearly-degenerate transitions. The width (~5,000 cm^{-1}) of the absorption appears too large for one electronic transition alone, consistent with this assignment. Hence, the structure is assumed to result from both the electronic multiplicity and vibrational coupling.

The magnitude ($\Delta A/A \sim 1\times10^{-2}$) and dispersion of the MCD together indicate that paramagnetic C terms predominate[1–4]. These arise from differential population of the sublevels of a degenerate ground state split by a magnetic field. Such terms are expected for metXbCN (X=M,H), because the ground state is a Kramers doublet. Their calculation requires the ground state g values, which are known from e.p.r. measurements, and electric dipole transition matrix elements. We have made such a calculation using standard MCD theory and a number of reasonable approximations. Following Shulman *et al.*[16] the iron d and porphyrin π molecular orbitals are assumed to approximate their form in D_{4h} symmetry. Using the e.p.r. data and ground state wave functions reported by Shulman *et al.*, we then obtain for transitions to excited states which are both $^2A_{1u}$ and $^2A_{2u}$ in D_{4h} symmetry

$$\frac{\Delta A}{A} \approx + \frac{g_z\beta H}{2kT}$$

where g_z is the component of the ground state g tensor perpendicular to the porphyrin plane, β is the Bohr magneton, H is the magnetic field strength in the direction of the light beam, k is Boltzmann's constant and T is the absolute temperature. With $g_z=3.4$ (ref. 16), and at 39.2 kG and 25° C equation one predicts $\Delta A/A \approx 1.5\times10^{-2}$. The experimental value of $\Delta A/A$ is nearly constant throughout the near IR bands and in good agreement in both sign and magnitude with the predicted value for $^2A_{1u}$ and $^2A_{2u}$ upper states. The MCD data thus strongly support the porphyrin-to-iron charge-transfer assignment. Because the two electronic transitions are predicted to have the same $\Delta A/A$, the MCD does not provide a means of further analysing the structure of the bands.

We have also measured the CD and MCD of the ferric high-spin derivatives metHb and metMb which each exhibit a broad absorption band at ~1,000 nm[13]. Again the CD is undetectable while the MCD is large. The shape of the MCD is quite different, however, from that in the low spin cyanide derivatives. Thus, not only can the MCD assist in the theoretical analysis of the near IR spectra of haemoproteins, but it can also provide a sensitive and diagnostic indicator of their spin states. The latter should make MCD a very useful analytical tool in the study of haemoproteins.

A more detailed discussion of the work outlined here will be presented elsewhere. We are currently extending our studies of haemoproteins and also investigating applications of IR CD and MCD to other biological systems.

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Halogenated Hydrocarbons in and over the Atlantic

DURING the past few decades the production of the chlorofluorocarbons, the propellant solvents for aerosol dispensers, has grown exponentially. R. L. McCarthy (unpublished) estimates that the integrated production of CCl_2F_2 and of CCl_3F, the two principal compounds of the class, was about one megaton of each in mid 1971; they are unusually stable chemically and only slightly soluble in water and might therefore persist and accumulate in the atmosphere. Preliminary tests in 1970 showed that CCl_3F was present in the air over Ireland at concentrations exceeding 10^{-11} by volume[1].

The presence of these compounds constitutes no conceivable hazard; indeed the interest lies in their potential usefulness as inert tracers for the study of mass transfer processes in the atmosphere and oceans. The voyage of the RRS Shackleton from the United Kingdom to Antarctica and back in 1971–72 provided an excellent opportunity to compare the observed global distribution of CCl_3F with the predicted distribution from models of the behaviour of an ideal inert gas. Additionally the apparatus used gave simultaneous measurements of two unexpected halomethanes: methyl iodide and carbon tetrachloride. These two compounds and CCl_3F were uniformly distributed both in air and sea.

Analysis was by gas chromatography. A novel electron capture detector capable of coulometric (absolute) measurements was used[2]. Air and seawater samples were taken several times daily and analysed directly; our observations are summarized in Table 1 and Figs. 1 and 2.

Table 1 Detected Levels of Halogenate Hydrocarbons

	CCl_3F	CH_3I	CCl_4
Mean aerial concentration $\times 10^{-12}$	49.6 (7.1)	1.2 (10.0)	71.2 (6.86)
Mean surface water concentration ml. ml.$^{-1}$ water (NTP)	7.6 (7.2)	135 (248)	60 (17)
Annual production rate (megatons)	0.44	40	1.7
Residence time (yr)	>10?	0.003	1

Figures in parentheses are standard deviations.

The release of CO_2 by combustion has been described as an unscheduled geophysical experiment; if so it is a rather undisciplined one, because emissions are small compared with those of the large complex natural cycle. By contrast the emissions of CCl_3F, also unplanned, are much closer to an ideal experiment on a global scale. There are no natural sources; it is chemically and physically inert; it does not disturb the environment, and can be measured accurately to one part in 10^{12} by volume.

A numerical model of the global atmospheric distribution of an ideal inert gas in space and time was developed by Machta[3]. In this, the gas was released at an exponentially growing rate with a doubling time of two years in the Northern Hemisphere between latitudes 35° and 55°. The CCl_3F observations are compared with Machta's predictions in Fig. 1 by making the centre point of the model distribution equal to the calculated global mean concentration. The latter comes from the division of the mass integral of CCl_3F production up to the end of 1971 (1.2×10^{12} g) by volume of the atmosphere. The observed and predicted global mean concentrations, 48 and 53 respectively, are in close agreement. That the observed distribution is shallower than the theoretical curve could be due to the difference between the doubling time of the emissions, 3.5 yr and the value of 2 yr used in the model. Except in the north temperate regions the surface waters were not in saturation equilibrium with the air. A few measurements down to 300 m at latitude 29° and 14° N showed a decline in concentration with an e^{-1} depth of 130 m.

Biological methylation is a ubiquitous tendency[4]; nevertheless it was surprising to find a familiar organic chemical reagent distributed throughout the oceans. The large difference between air and sea concentrations (Table 1) suggests the sea to be a source. There was no obvious change of concentration with latitude, although there were large local variations; in a separate investigation one of us (J. E. L.) has found marine algae to be a strong source of CH_3I and it seems probable that the origins of this compound are in the oceans and are biological. The atmospheric residence time of methyl iodide has been estimated by Eggleton and Clough (unpublished work) as 50 h; they assumed photolysis in sunlight to be the sole destructive process. This estimate, taken with the mean aerial concentration of 1.2×10^{-12}, implies an annual production of 40 megatons. We suggest that methyl iodide is the natural carrier of iodine between the seas and the land fulfilling a role for this element similar to that proposed for sulphur by dimethyl sulphide[5].

The presence of carbon tetrachloride in the air is only slightly more unexpected than is its distribution with latitude shown in Fig. 2. Chlorinated hydrocarbons found in the natural environment are almost always assumed to come from chemical industry, but the aerial concentrations of CCl_4 in the southern tropical regions were as high as those of the northern temperate regions and this is inconsistent with an industrial or domestic source. A few measurements to 300 m showed a decline in CCl_4 concentration with an e^{-1} depth of 50 m. This is a steeper decline than that of CCl_3F, and suggests the hydrolysis of CCl_4 and that the sea is a sink. A single sample of air collected in the stratosphere (provided by D. H. Ehalt) showed CCl_4 to be present there at one fifth the concentration of the upper troposphere; this, taken with the observed concentration minima in the region of the Azores high and the St Helena high, suggests that the stratosphere may also be a sink. The slight fall in aerial concentration seen on going south could be due to some increment from chemical industry but also might be a consequence of the greater area of sea in the south to act as a sink.

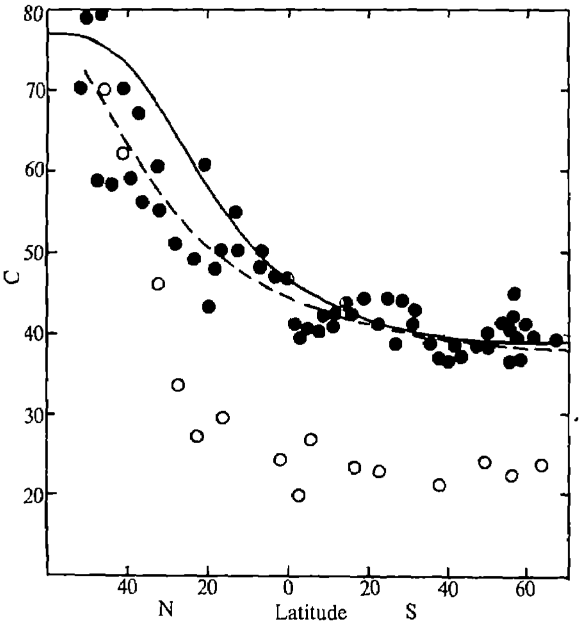

Fig. 1 Distribution of CCl_3F in and over the North and South Atlantic Ocean. ●, Aerial concentrations ($\times 10^{-12}$) by volume. ○, Seawater concentrations ($\times 10^{-12}$); as aerial concentrations in equilibrium with water. ——, Theoretical prediction. ---, Best fit third degree polynomial.

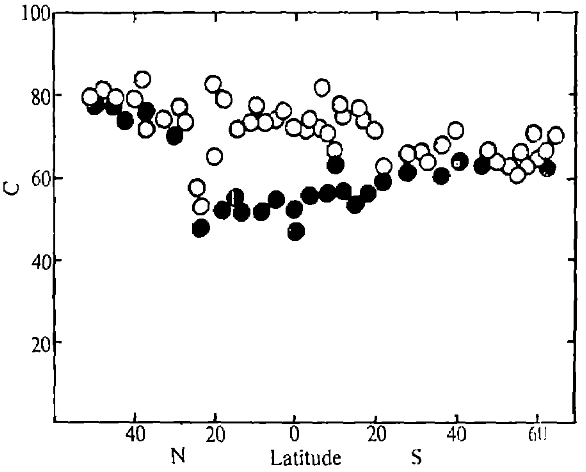

Fig. 2 ●, Aerial distribution of CCl_4; ○, marine concentration ($\times 10^{-12}$) by volume. Water concentration ($\times 10^{-12}$) as aerial concentration in equilibrium with water

The total annual industrial production of CCl_4 is about one megaton of which 95% is used to make CCl_3F and similar compounds. This leaves a maximum of 20 kilotons to escape to the air. Junge[6] has proposed a method for estimating the approximate residence time of an atmospheric component based on the inverse correlation between residence time and standard deviation of the aerial concentration. From this the residence time of CCl_4 would be about 1 yr, and the annual production rate 1.9 megaton. This is far in excess of any possible industrial source and raises the intriguing problem of the nature of the atmospheric or surface reactions leading to this unlikely product.

All three gases were found in the air and in the sea wherever and whenever they were sought. It is true that the concentrations, less than parts per 10^{10} by volume, were very low and that but for the sensitivity of the analytical technique used they might never have been detected. These low concentrations belie the interest and importance of the three compounds as atmospheric components. They are each an uncomplicated representative of a separate class of compound; CCl_3F is one of the few substances present and easily measured in the air which is wholly anthropogenic in origin; other emissions from the domestic and industrial sector such as the oxides of carbon and sulphur are also components of the natural environment. The unique source and its stability in the air make it an ideal reference substance against which man's other emissions to the environment can be compared. CH_3I is probably a singular product of marine biology and may be a key compound in the natural cycle of iodine between the seas and the land. In spite of its low aerial concentration, the atmospheric throughput is tens of megatons in each year. CCl_4 seems very likely to be a product of natural inorganic chemistry, possibly the reaction of methane in the troposphere with chlorine in a complex sequence of reactions. This substance also is passed through the environment in quantities exceeding 1 megaton annually. In view of the concern over pollution by chlorinated hydrocarbons it is at least consoling to discover that one of them is a natural product.

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Variations in Hydrocarbon Gas Concentration during Supertanker Cleaning Operations

FOLLOWING recent serious explosions aboard very large crude carriers (VLCC), investigations into the possible causes of such accidents have been initiated in a number of countries. Initially, interest was focused on the problems of cleaning and gas freeing of cargo tanks, especially with rotating jet washing machine systems, the electrostatic hazards of which have been reported[1].

Two requirements for ignition of a hydrocarbon gas mixture in a cargo tank are generation of sufficient energy and a tank atmosphere within the flammable range. Before 1960, published information was scarce regarding the explosive conditions which may occur in a tank and the ways in which a tank may be treated during a ballast voyage. In 1960, investigations were reported[2] that justified a large scale trial of the method of forced ventilation of cargo tanks before and during tank cleaning (the too lean method). Overall results were successful[3], and this particular system of tank cleaning has been employed over a number of years aboard Shell ships from 50,000 to 110,000 d.w.t.

However, in December 1969 three VLCCs had serious explosions in one of their centre tanks during tank cleaning. Two of the ships were members of the Shell Group Fleet, M/T Marpessa and M/T Mactra, both 220,000 d.w.t., and the third was the Norwegian ship King Haakon VII, 219,000 d.w.t. While the two Shell tankers had been employing the too lean method for tank cleaning, the Norwegian ship had followed the still quite common practice with no ventilation before or during tank cleaning.

Several of the following investigations[4-7] confirmed the earlier results[2,3], indicating that during a ballast passage, the tank atmospheres on crude vessels, large or small, during tank washing, or empty on passage, may at any time be within the flammable range. Over-rich atmospheres were found to be the exception rather than the rule.

Since September 1970 we have been investigating various aspects of explosion hazards aboard VLCCs. Here we discuss some of the results obtained by exact measurements of gas concentrations aboard a VLCC, T/T Tabriz (210,000 d.w.t.), before and after unloading of Kuwait medium crude oil as well as before, during and after tank cleaning operations. Gas samples were drawn through rubber tubes, usually from 10, 40 and 70 foot levels below deck and both in the forward and aft sections of the tanks. The concentrations of each of the hydrocarbon gases from methane to hexane in the gas samples were determined by gas chromatography (GC) using a flame ionization detector (FID) and a 24 foot × 1/8 inch i.d. copper tubing packed with 20% di-isodecylphthalate on 80–100 mesh 'Chromosorb W' as the chromatographic column. The column readily separates the C_1–C_6 hydrocarbons which are determined using response curves obtained with pure standards. Hydrocarbon gas compositions are expressed in per cent by volume.

We summarize the essential results from our measurements in one of the wing tanks, port tank No. 1 (14,555 m^3). The values reported from the empty tank refer to gas samples drawn from 40 foot below deck in the middle section of the tank.

Fig. 1 shows the variations in the total hydrocarbon gas concentration from the time of unloading until ventilation and washing. The uncleaned empty tank remained in the explosive range during the first days after unloading, and the total hydrocarbon gas concentration increased with time owing to gassing from oil deposits on the walls and in the bottom of the tank. Forced ventilation brought the hydrocarbon gas concentration well below the lower explosion limit (l.e.l.) before the washing operation was started. We made continuous measurements during washing, and our results (Fig. 1, inset) show a marked increase in the total gas concentration when washing was started and the subsequent reduction due to the continued ventilation.

We also found that changes in the composition of the hydrocarbon gas mixture in the ullage and in the empty tank before and during washing were very pronounced (Fig. 2). In the ullage, the two dominating hydrocarbon gases are propane and butane, and both are present in concentrations of approximately 7.5% volume out of a total of approximately 19% volume. When the tank is empty but before ventilation and

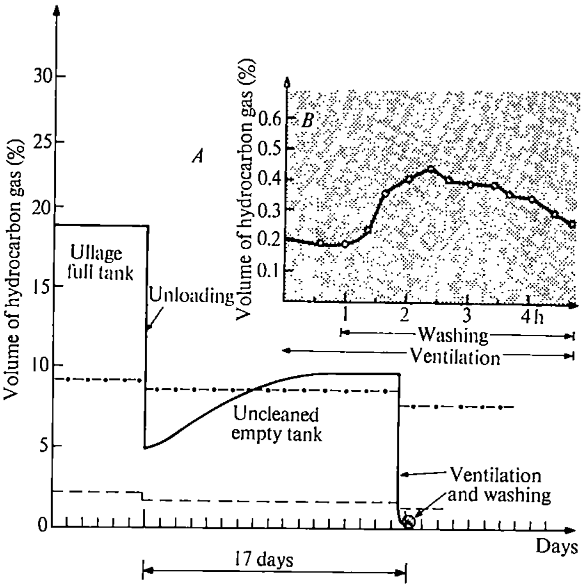

Fig. 1 *A*, Schematic drawing of the variations with time in the hydrocarbon gas concentration (——), the upper explosion limit u.e.l. (—O—O) and the lower explosion limit l.e.l. (- - -) in port wing tank No. 1. *B*, The variations with time (h) in the hydrocarbon gas concentration during the ventilation and washing periods, enlarged.

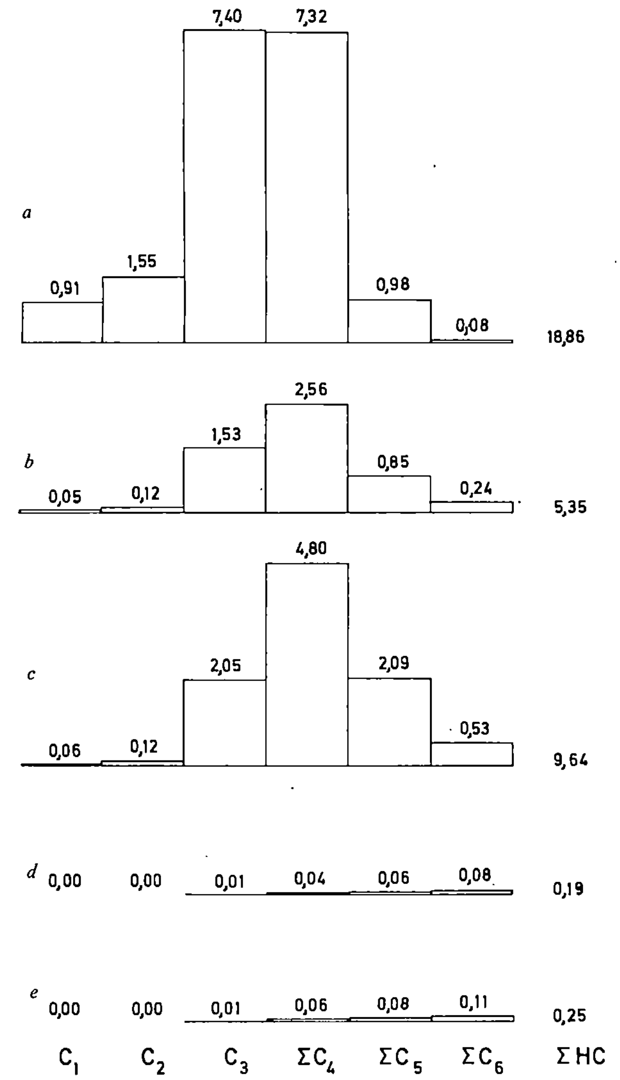

Fig. 2 Typical variations in hydrocarbon gas concentration in the ullage and in the empty tank before and during washing (C_1=methane, C_2=ethane, C_3=propane, ΣC_4=butanes, ΣC_5=pentanes, ΣC_6=hexanes, ΣHC=total hydrocarbon gas concentration, all values in volume % gas). *a*, Before unloading. *b*, After unloading. *c*, Before ventilation. *d*, Beginning of washing. *e*, End of washing.

washing, butane is the major constituent followed by propane and pentane, with methane and ethane present in negligible concentrations. By the end of the washing period, the major constituents of the tank atmosphere are hexane and pentane.

These changes in the composition of the hydrocarbon gas mixture also result in variations in the values of the lower (l.e.l.) and the upper explosion limits (u.e.l.) of the mixture in air (Fig. 1). In the ullage, the l.e.l. is 2.09% volume, while the u.e.l. is 9.43% volume. By the end of the washing period, the l.e.l. is 1.36% volume, while the u.e.l. is 7.88% volume.

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Relation of Pleistocene Migrations of Pygmy Stegodonts to Island Arc Tectonics in Eastern Indonesia

PLEISTOCENE pygmy stegodonts have been described from the Indonesian islands of Sulawesi, Flores and Timor[1–4] which are now separated by deep seas. Hooijer[4] suggested that the two forms *Stegodon trigonocephalus florensis* and *Stegodon timorensis* apparently coexisted in Flores as well as in Timor, although they may not have been strictly contemporaneous. He concluded that the dwarfing *Stegodon* populations wandered back and forth between Flores and Timor during the Pleistocene, because otherwise it is hard to see how the two evolutionary products on Timor and Flores could have been so similar. Flores is now separated from Timor by a 3,000 m deep Savu Sea 150 km wide which narrows to 30 km in the Ombai Strait between Alor and Timor (Fig. 1). Because an elephant (and presumably a stegodont) could not swim across the Savu Sea and Ombai Strait, the existence of a land connexion between Flores and Timor during the Pleistocene must be postulated (Fig. 1).

The suggestion of a land connexion between northern Timor and the chain of volcanic islands of Flores, Alor and Wetar is supported by the stratigraphy of the Viqueque Formation in northern Timor[5]. The lower members of the Viqueque Formation, which range in age from late Miocene to late Pliocene (equivalent to the planktonic zones N.18–N.21 of Blow's scheme[6]), consist of a basal part deposited in a relatively deep open sea and an upper part deposited in a much shallower sea near the shore. This indicates that the Pliocene sea which covered large parts of Timor became much shallower in the late Pliocene. The older members of the Viqueque Formation are widely distributed in Timor, but the bulk of the formation, which is of Pleistocene age (equivalent to zone N.22 of Blow's scheme[6]), is not developed anywhere in northern Timor (Fig. 2). This large break in the Viqueque succession is a feature of northern Timor where the basal facies of Pliocene age is overlain unconformably by the late Pleistocene and Holocene terraces of reef limestones or alluvium[5,7,8]. The lower and middle Pleistocene marine deposits absent from northern Timor are extensively developed in other parts of the island[5,7]. Their absence implies that northern Timor was above sea level during at least part of the early and middle Pleistocene.

Except for the occurrence of the pygmy stegodonts in Flores and Timor there is no available geological evidence to demonstrate that this Pleistocene land area in northern Timor connected with the Inner Banda Arc. It is not necessary to postulate that the entire region between Timor and Flores was land; pygmy stegodont migrations might have taken an indirect route *via* Alor. The Ombai Strait between Alor and Timor offers much the shortest route for migrations between the Inner and Outer Banda Arcs (Figs. 1 and 2), and the glacial lowering of sea level may have been a critical factor in establishing a land connexion between these regions during the early and middle Pleistocene.

It has been argued[9] that the late Pliocene-early Pleistocene orogenic phase in Timor resulted from a collision between Australian continental crust (which extended north of Timor) and a subduction zone which lay south of the volcanic island chain of Flores, Alor and Wetar. The absence of recent volcanic activity in Alor, Atauro, Wetar and Romang islands of the Inner Banda Arc, that are closest to Timor[10], may be associated with the apparent cessation of subduction in this part of the Banda Arcs[11,12]. We have postulated that a period of uplift in this region between the Inner and Outer Banda Arcs occurred directly after the orogenic folding phase in the early Pleistocene, on the basis of evidence from the Viqueque Formation and the distribution of pygmy stegodonts. Such uplift could be expected to follow the cessation of subduction in a zone where all available oceanic crust had been subducted[9] (Fig. 1).

The presence of the Savu Sea, Ombai and Wetar Straits, now all more than 3,000 m deep, in a region that we suggest was partly land in the middle Pleistocene, implies that late Pleistocene and Holocene downfaulting occurred between the Inner and Outer Banda Arcs. The vertical displacements involved are at least 3,000 m. After the middle Pleistocene Timor and the volcanic island chain of Flores, Alor and Wetar have been uplifted, as indicated by raised terraces, often covered by reefs, up to 765 m in Timor[5,10], 250 m in Flores, 700 m in Alor and 820 m in Wetar[10]. The deeply incised alluvial terraces of these islands (from which the stegodont bones were obtained[1,3,4]) also indicate this recent uplift.

Hooijer[3] recently concluded that there are two species of *Stegodon* in Sulawesi; a pygmy species *Stegodon sompoensis* very similar to *Stegodon timorensis* of Flores and Timor and the *Stegodon trigonocephalus* similar to the much larger Java species. This discovery of large and pygmy species in Sulawesi raises the possibility of Pleistocene migrations of dwarfing populations between Java, Flores and western Sulawesi.

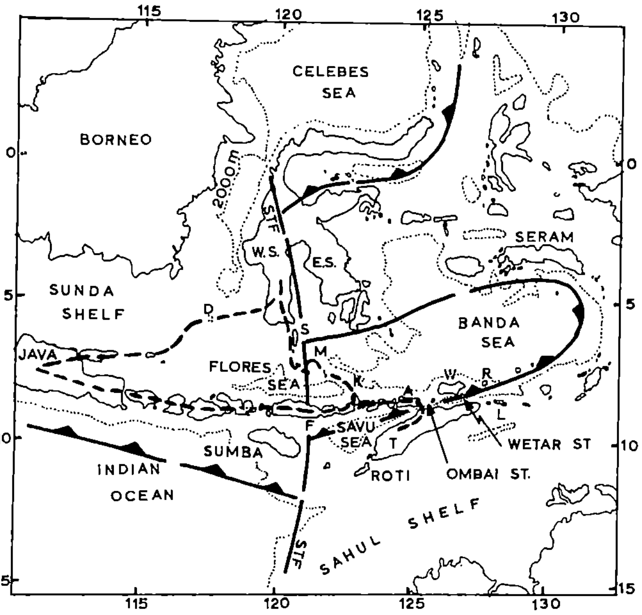

Fig. 1 Map of eastern Indonesia to show postulated Pleistocene migrations of stegodonts. In the Celebes Sea and Makassar Strait the 2,000 m bathymetric contour has been drawn, but elsewhere only the 3,000 m contour is shown. WS, Western Sulawesi; ES, eastern Sulawesi; S, Salajar Is; M, Matjan Is; K, Kaloatoa Is; D, Doangdoang shoals; F, Flores; A, Alor; W, Wetar; R, Romang; L, Leti; T, Timor; STF, Sarasina transform[9]. ---, Stegodont migrations; ▲ , early Pleistocene plate margin; ▲, indicates subduction.

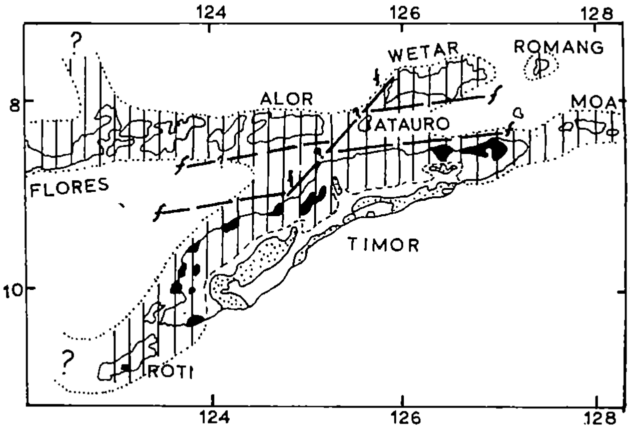

Fig. 2 Map of part of the Lesser Sunda Islands to show (vertical stripes) the early and middle Pleistocene land areas of northern Timor and their postulated connexion with the Inner Banda Arc. The postulated position of recent faults which have dropped the floor of the Savu Sea, Ombai and Wetar Straits by at least 3,000 m are indicated. The outcrop of the important Pleistocene diastem in the Viqueque is shown (in black). The dotted areas represent thick Pleistocene marine Viqueque Formation deposits.

At present south-west Sulawesi is connected to the north-east tip of Flores by a submarine ridge nearly 3,000 m deep that separates the Flores and Banda Seas (Fig. 1). The early and middle Pleistocene uplift, that we suggest affected Timor and the Flores-Wetar region, may have extended northwards to allow the pygmy stegodonts to wander back and forth between Flores and Sulawesi along the Kaloatoa-Matjan ridge, then *via* Tanahjampea and Salajar ridge. This ridge system may also have been elevated above sea level by a regional uplift that followed the plate collision between eastern and western Sulawesi in the late Pliocene-early Pleistocene[9]. Another land connexion may have developed, as a result of glacial lowering of sea level, across the Sunda Shelf (now 200 m deep) from Java *via* the Doangdoang shoals to Makassar in western Sulawesi. If these were the stegodont migration routes they imply late Pleistocene and Holocene down-faulting of the Flores Sea and southern Makassar Strait, analogous with the postulated recent down-faulting in the Savu Sea, Ombai and Wetar Straits, which followed the uplift that occurred after continental crust of the Australian plate collided with a subduction zone[9].

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BIOLOGICAL SCIENCES

Geographical Uniformity of Protein Polymorphisms

ELECTROPHORETIC polymorphisms in several species of *Drosophila* in both North and South America and in Europe show considerable uniformity of allele frequencies over a wide geographical range[1-3]. It has been suggested by Kimura and Ohta[4] that this finding is compatible with the infinite neutral allele hypothesis of Kimura and Crow[5] as "it is possible that in animal species such as *Drosophila*, mouse and man well able to migrate, no local population is sufficiently isolated to prevent the entire species or subspecies from forming effectively one panmictic unit". This claim is supported by reference to the theoretical work of Maruyama[6,7] on the asymptotic rate of decrease of heterozygosity in the absence of mutation, which would seem to be of little relevance to the pattern of variability expected under the joint forces of mutation and genetic drift. Here I show that use of a more appropriate model, which includes the effect of mutation, leads to a quite different conclusion.

Malécot[8] has made a theoretical study of the coefficients of inbreeding and kinship under a continuous, two-dimensional dispersal model. He implicitly defines the coefficient of inbreeding, f_0, as the probability that two homologous loci in an individual are identical by descent and that neither of them has undergone mutation since the common ancestor from whom they arose. The coefficient of kinship, f_x, between two individuals at a distance x apart is defined in a similar way. This definition of the coefficients of inbreeding and kinship, which takes mutation into account, circumvents the difficulty encountered in the usual definition, which ignores mutation, that if one traces genes back far enough all genes are from a common ancestor so that every individual is completely inbred. Under the usual definition inbreeding must always be taken relative to a fixed point in the not too far distant past, but under Malécot's definition it is sensible to consider an equilibrium of inbreeding relative to the very distant past. His definition is most easily interpreted under the infinite neutral allele hypothesis since in this case any mutation must be to a new allele not already present in the population. It follows that f_0 can be interpreted as the probability of homozygosity and f_x as the probability that two alleles chosen at random from individuals at a distance x apart are identical in state.

Malécot[8] has shown that an approximate formula for f_0 is

$$f_0 = [1+4\pi\sigma^2\delta/\ln(1/2u)]^{-1} \tag{1}$$

where σ^2 is the mean square dispersal distance between the breeding places of parent and offspring, δ is the density of the breeding population and u is the mutation rate per gene per generation. An approximate formula for f_x, valid for $x>\sigma$, is

$$f_x = \frac{(1-f_0)}{2\pi\sigma^2\delta} K_0(2\sqrt{u}x/\sigma) \tag{2}$$

where K_0 is a modified Bessel function of the second kind. These formulae are valid whatever the shape of the dispersal distribution. If we define $\rho_x = f_x/f_0$ as a measure of the correlation between individuals (or populations) at a distance x apart, it follows that

$$\rho_x = 2K_0(2\sqrt{u}x/\sigma)/\ln(1/2u) \tag{3}$$

This quantity depends only on the mutation rate, u, and on the standardized distance, x/σ, expressed in units of the root mean square dispersal distance. Numerical values of ρ_x are given in Table 1.

These results can be used to test the infinite neutral allele hypothesis from observed data on the geographical uniformity of protein polymorphisms. If $p_{ij}(A)$ is the observed frequency of the j^{th} allele at the i^{th} locus at locality A, the chance that a gene chosen at random from locality A will be identical in state with a homologous gene chosen at random from locality B can be estimated by $\sum_{i,j} p_{ij}(A)p_{ij}(B)/n$, where n is the number of loci examined, whereas the chance of homozygosity of an individual chosen at random with equal probability from A or B can be estimated by $\sum_{i,j}(p_{ij}^2(A)+p_{ij}^2(B))/2n$. The ratio of these two quantities, r_{AB}, is thus an estimate of ρ_x. Values of r have been calculated in this way for the three non-isolated populations of *Drosophila pseudoobscura* studied by Prakash, Lewontin and Hubby[1]. Of the 24 loci studied 14 were found to be polymorphic in at least one population, while 10 loci were fixed at the same allele in all populations; r has been calculated using only the 14 polymorphic loci and also using all 24 loci. The results are shown in Table 2. These results cannot be reconciled with the theoretical predictions shown in Table 1 except under the absurd assumption that the root mean square dispersal distance, σ, is of the order of 2,000 km.

Table 1 Theoretical Values of ρ_x

x/σ \ u	10^{-4}	10^{-5}	10^{-6}	10^{-7}
1	0.95	0.96	0.96	0.97
2.5	0.73	0.79	0.83	0.85
5	0.57	0.66	0.72	0.76
10	0.41	0.53	0.61	0.67
25	0.22	0.37	0.47	0.55
50	0.10	0.24	0.37	0.46
100	0.03	0.14	0.27	0.37
250	0.00	0.04	0.14	0.26
500	0.00	0.02	0.06	0.17
1,000	0.00	0.00	0.03	0.10

Another difficulty with the infinite neutral allele hypothesis is that it predicts a degree of heterozygosity in excess of the observed amount. The average heterozygosity found by Prakash *et al.*[1] in the three non-isolated populations considered in Table 2 is 0.123. Equating this figure to $1-f_0$, with f_0 defined in equation 1 and with $u=10^{-5}$, shows that $\pi\sigma^2\delta=0.38$. But $\pi\sigma^2\delta$ is the number of flies within a circle of radius σ, and to make this number less than 1, σ would have to take an absurdly small value, whereas it has been shown in the preceding paragraph that to account for the geographical uniformity σ must take an absurdly large value. A way out of this dilemma would be to suppose that the population had increased fairly recently and not yet reached an equilibrium level of heterozygosity; to explain the geographical uniformity it would also be necessary to suppose that the whole present population had spread from a single centre of dispersion. The fact that a similar amount of heterozygosity with considerable geographic uniformity has been found in different species in different parts of the world, however, makes this explanation unlikely.

Table 2 Estimated Values of r for *Drosophila pseudoobscura*

Pair of populations	Distance (km)	r (polymorphic loci)	r (all loci)
S and M	1,200	0.985	0.992
S and A	2,400	0.981	0.990
M and A	1,250	0.995	0.997

S—Strawberry Canyon, Berkeley, California.
M—Mesa Verde, Colorado.
A—Austin, Texas.

An alternative to the infinite neutral allele hypothesis is to suppose that there is only a small number of neutral alleles at each locus, but that the effective population size is large enough for mutation pressure to maintain considerable heterozygosity at these alleles. To explain geographical uniformity under this model it is necessary to suppose that the effective population size is large enough to make drift negligible, so that the allele frequencies are close to their equilibrium values. If a locus is considered with two neutral alleles with forward and backward mutation rates μ and ν, the equilibrium gene frequencies of these alleles are $P=\nu/(\mu+\nu)$ and $Q=\mu/(\mu+\nu)$ respectively. Under the same continuous two-dimensional dispersal model as before it has been shown by Malécot[9] (using a more direct argument not dependent on identity by descent) that the variance in gene frequencies between very distant populations is f_0PQ, and that the correlation in gene frequencies between populations at a distance x apart is ρ_x, where f_0 and ρ_x are as defined in equations 1 and 3 except that $(\mu+\nu)$ must be substituted for u. (It must be remembered that μ and ν are mutation rates per nucleotide rather than per cistron.) If p_A and p_B are gene frequencies in two populations at a distance x apart, it follows that the expected value of $\frac{1}{2}(p_A-p_B)^2$, which may be taken as a measure of the variability of gene frequencies between these two populations, is $f_0(1-\rho_x)PQ$. In order that this quantity should be small it is necessary for f_0 to be small, say less than ε, which implies that $\pi\sigma^2\delta$ is greater than $-(1-\varepsilon)\ln[2(\mu+\nu)]/4\varepsilon$; for example, if $(\mu+\nu)=10^{-7}$ I postulate that $\pi\sigma^2\delta>382$ to make $f_0<0.01$. It does not seem unreasonable to suppose that the number of flies within a circle of radius σ should be of this order of magnitude. The effect of balancing selection can be approximately incorporated into the above model by adding the linearized selection pressure to $(\mu+\nu)$; for example, if the two homozygotes are at selective disadvantages s_1 and s_2, the quantity $s_1s_2/(s_1+s_2)$ should be added to $(\mu+\nu)$[10]. Only a very weak selection pressure need be postulated to explain the observed polymorphisms.

I conclude that data on electrophoretic polymorphisms in *Drosophila* are inconsistent with the infinite neutral allele theory of Kimura and Crow[5], but that they are consistent with the existence of a small number of alleles at each locus which are either neutral or subject to balancing selection. The geographical uniformity of these polymorphisms shows that the effect of genetic drift is negligible, so that all the neutral or heterotic alleles are maintained near their equilibrium gene frequencies.

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Ancient Chromosomal Polymorphism in Hawaiian *Drosophila*

POLYMORPHISM due to inverted chromosome segments is known in natural populations of many living species, including man[1,2]. A specific inversion arises in one member of a monomorphic chromosome pair and is apparently monophyletic. Where fine-scale mapping of the breaks is possible, as in giant polytene chromosomes, an indelible marker, unique in the history of the species, is produced. Accordingly, in favourable geographical circumstances, inversions can be used as tracers of ancient populations[3]. Such precision is not possible with visible mutations or electrophoretically detected variants.

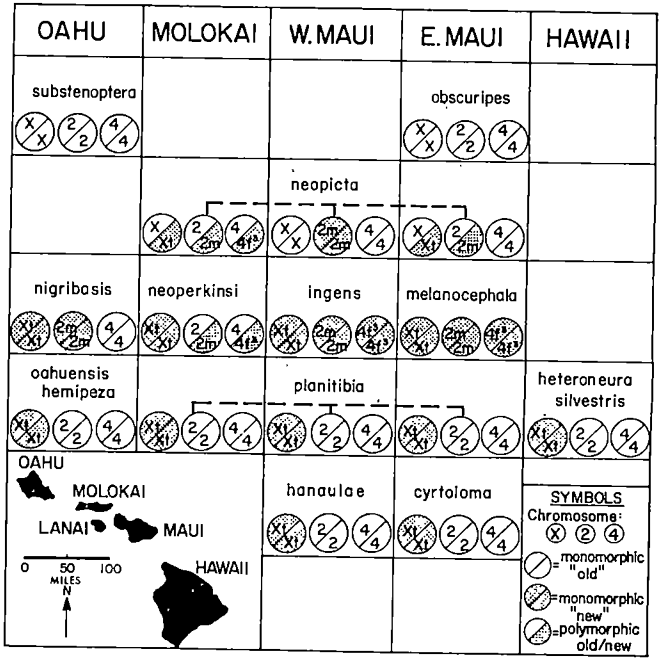

Fig. 1 Geographical distribution and relevant chromosomal conditions in fourteen large *Drosophila* species found on four southeastern Hawaiian islands. For details see text.

After an inversion has occurred, there exist two alternate arrangements of genes. In the case of a naturally-occurring polymorphism, the ancestral and derived arrangements cannot be recognized by any intrinsic property of the chromosome itself. The "oldness" of one of the alternates must be established in some other manner.

I wish to describe a method of establishing these relationships for particular polymorphisms, based on data from a species endemic to the Hawaiian Islands, *Drosophila neopicta*. Most of the data on which these formulations are based have been published[4,5]. The giant chromosomes of ninety-six closely related species of Hawaiian *Drosophila* (the "picture-winged" group) have been mapped[6]. The sequential karyotypes of each species and its polymorphisms have been described in terms of an arbitrary standard (*Drosophila grimshawi*). Among these species, 198 inversions have been found. Many of these (123) have never been found in the polymorphic state within any species; they are recognized by inspection of the banding order in the homozygous state. Because of the exceptional quality of the chromosomes of this group, recognition of the interspecific homology of all banded regions of each of the five major polytene chromosomes is possible.

An important feature of these data is that it is possible to determine, by direct cytological examination, whether a species has, or does not have, a particular banding sequence in one or more sections of its karyotype. I shall focus attention on three of the eight polymorphisms known in populations of *D. neopicta*. These are designated X/Xt, $2/2m$ and $4/4f^3$; each difference is due to a single inversion in chromosomes X, 2 and 4 respectively. The geographical distribution of this species and of the above three pairs of alternate gene arrangements is given in Fig. 1 (upper centre). The samples are small (6 to 18 chromosomes from each of the three volcanoes) so that the absence of polymorphism in several instances may not be significant.

The question arises: is it possible to recognize any of these alternate gene arrangements as derived? Evidence that Xt, $2m$ and $4f^3$ are derived exists (Table 1). Xt is fixed in eleven species but is lacking in eighty-four; this statement is based on a large number of chromosome examinations[5,6].

The standard X segment is found in a diversity of species belonging to five subgroups of the picture-winged *Drosophila*.

Table 1 Three Chromosomal Polymorphisms found in *D. neopicta* and Distribution of the two Gene Arrangements Comprising each Polymorphism (X/Xt; $2/2m$; $4/4f^3$) in Ninety-five Related Hawaiian Species

	Species or chromosomal subgroup	No. of species	N_A	N_X	Gene arrangement present (+) or absent (−) X	Xt	2	$2m$	4	$4f^3$
(I)	Grimshawi	56	2,765	2,075	+	−	+	−	+	−
(III)	Adiastola	14	422	330	+	−	+	−	+	−
(IV)	Punalua	8	392	303	+	−	+	−	+	−
(V)	Primaeva	2	94	68	+	−	+	−	+	−
(II)	Planitibia (in part: *D. picticornis*, *D. setosifrons*, *D. substenoptera*, *D. obscuripes*)	4	186	142	+	−	+	−	+	−
	D. neopicta	1	36	29	+	+	+	+	+	+
	D. neoperkinsi	1	12	10	−	+	+	+	+	+
	D. nigribasis	1	16	12	−	+	−	+	+	−
	D. ingens and *D. melanocephala*	2	18	13	−	+	−	+	−	+
	Remainder of (II) Planitibia subgroup (see Fig. 1)	7	180	144	−	+	+	−	+	−
	Total	96								

N_A, N_X, No. of autosomes and X chromosomes observed.

Among these are the two species of the *primaeva* subgroup. These latter are primitive and are found on the geologically old island of Kauai. They are intermediate in phylogenetic position between the picture-winged species of the newer Hawaiian islands and certain Palearctic and Nearctic continental forms, notably the *robusta* group[7-9].

In contrast, the Xt inversion is found only among twelve closely related species of the *planitibia* subgroup, most of which are endemic to the geologically recent (<1.5 m.y.[10]) islands of Molokai, Maui and Hawaii (Fig. 1). The subgroup has sixteen members, fourteen of which are unusual in *Drosophila* in that they have an extra cross-vein in cell R-5 of the wing. These features and the distribution of the species suggest their recently-evolved, terminal position in the general phylogeny of the picture-winged species[5].

The facts concerning the two autosomal polymorphisms supplement those for the X chromosome. Thus, the same eighty-four species which lack Xt also lack arrangements $2m$ and $4f^3$. Accordingly, it may be concluded that standard segments X, 2 and 4 are ancestral and that Xt, $2m$ and $4f^3$ are derived. In Fig. 1, the circular symbols under the species' names reflect this: they are shaded if the gene arrangement concerned is derived and left open if it is ancestral.

Of the fourteen species considered in Fig. 1, only *D. substenoptera* (Oahu) and *D. obscuripes* (East Maui) are monomorphic for all three ancestral chromosomal types (top row; open circles). On the other hand, one or more new inversions are found in the monomorphic state in eleven species (lower three rows; shaded circles, Fig. 1). Each of these latter species must have had, as an ancestor, a population that was at first monomorphic for old chromosomes. Later, the ancestor must have become polymorphic "old/new". Accordingly, the facts suggest that these eleven species are newer than those which are polymorphic old/new. It is not possible to designate any living species as the most primitive in this series. This is because of the possibility of refixation, in a modern species, of an old chromosome from an old/new polymorphism in its ancestor.

Conditions in *D. neopicta* are especially instructive. Populations from Molokai have old/new polymorphisms in three chromosome pairs. *D. neoperkinsi*, a Molokai endemic sympatric with *neopicta*, has the same two autosomal polymorphisms. Only these two species carry old/new polymorphisms; the nine others having new arrangements carry them in the homozygous state.

The possibility needs to be considered that the old/new polymorphisms are due to recent hybridization rather than ancient polymorphism. The strongest evidence against this hypothesis is the fact that, among all the species of the *planitibia* subgroup on Molokai and Maui, *neopicta* is extraordinarily disparate in size, morphology and especially in mating behaviour (ref. 11 and unpublished results of H. Spieth). Thus, in contrast to the others, it is a small fly with poorly developed lek behaviour. On these grounds, matings may be considered unlikely. Each of the species is highly distinctive and each retains these characteristics in laboratory cultures.

The facts strongly suggest that all twelve existing species which carry new arrangements were ultimately derived from a singly, doubly or triply polymorphic ancestral population. The latter condition exists today in the *neopicta* population of Molokai. The proposed ancestral population was probably also a large one. Whereas most of the species under consideration here are geographically confined and chromosomally monomorphic, *neopicta* is widespread, suggesting that similar populations could have existed in the past. Also, if the putative ancestral population was continuously small, confined, and only lately expanded, it would seem unlikely that it could retain the three ancient polymorphisms over the geological time indicated. On the contrary, random drift would be expected to eliminate this variability.

Large, geographically widespread and chromosomally polymorphic populations seem to be unusual in the Hawaiian fauna. More than 70% of the picture-winged species are without any intraspecific chromosomal polymorphism; most have restricted distributions and seem to exist in small populations[5].

Genetic features of past populations have been inferred from conditions in descendant species by several authors[9,12,13]. The following view is consistent with these ideas. I suggest that certain large, highly heterozygous, long standing populations may be especially prone to produce small, semi-isolated, inbred populations on their margins. These latter may become species through peripheral isolation and the founder effect[3,14]. If the large population can survive over a long period it may remain competent for speciation and may continue to bud off new species while retaining its ancestral character. Only a few of the new species formed might acquire the wide distribution, large size and heterozygosity of their ancestor. The rest of the species, with small, geographically confined populations would be expected to be less competent for speciation.

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Hypotaurine: Regulation of Production in Seminal Vesicles and Prostate of Guinea-pig by Testosterone

THE accessory sex organs of the male are dependent on androgens for their growth, maintenance and secretory activity. These physiological effects are regulated through the RNA-protein biosynthesis system in the various animal species. The protein of the guinea-pig seminal vesicles, seminal fluid and prostates decreases after castration and increases after testosterone administration in direct proportion to the changes in tissue weights without change in amino-acid composition. The rate of incorporation into protein of 2-^{14}C glycine *in vivo*[2] and several ^{14}C amino-acids by cell free preparations of these tissues[3] is decreased by castration and increased by testosterone with concomitant changes in RNA[4].

As protein synthesis is dependent on the availability of the necessary amino-acids, the soluble fractions of these tissues were analysed for their respective amino-acids and other ninhydrin positive substances. The striking changes in the concentration of hypotaurine after castration and testosterone administration are presented here because of the implications with respect to fertility and other physiological and pathological changes in the prostate and seminal vesicles.

The guinea-pigs were castrated at approximately 3 months of age. Three weeks later two pellets of testosterone (approximately 15 mg each) were implanted subcutaneously[3,4] and the animals were killed after 23 day. The prostates and seminal vesicles were separated, cleaned of extraneous tissue and the seminal fluid removed from the seminal vesicles. The weighed organs were wrapped separately in aluminium foil, placed in a sealed plastic bag and frozen at −20° C. The coagulated seminal fluid was extracted immediately. The free amino-acids were extracted with 6 M $HClO_4$ essentially as described by Saifer[5]. Norleucine[6] was added at the beginning of extraction as an internal standard. The analyses were performed on a 'Beckman/Spinco Analyser, Model 120B'.

The concentration of hypotaurine and taurine in the seminal vesicles and prostate was much greater than that of the sulphur amino-acids (Table 1) and also of the common amino-acids and other ninhydrin-reacting compounds (unpublished). The hypotaurine in both tissues was drastically reduced by castration and restored by testosterone treatment. The concentration of taurine was not significantly altered by either treatment in the seminal vesicles and was slightly altered in the prostate while half-cystine and methionine were increased by castration and restored to or towards normal by the androgen except for a questionable effect in the cystine of the prostate. The hypotaurine in the normal seminal fluid was even greater (26.5 µmol g^{-1}) than in the tissue. Taurine, half-cystine and methionine, however, were approximately the same as in the tissue.

Hypotaurine is derived mainly from cysteine and is an intermediate in the production of taurine in the liver[7,8]. It is also produced in the fallopian tube of many animal species[9], ovaries of the ewe[9] and the sperm[10], and the fluid of the seminal vesicles and epididymis[11] of the boar. Production in the fallopian tube of the ewe increases during the latter part of the oestrous cycle when fertilization occurs, and decreases as the concentration of progesterone increases[11]. The administration of an anti-fertility agent, 6α-methyl-17α acetoxyprogesterone, also greatly inhibits hypotaurine production[12].

Van der Horst and Brand[9] suggest that the decreased fertility after administration of the anti-steroid is due to the decreased production of hypotaurine by the fallopian tube and attribute the beneficial effect of hypotaurine to its strong anti-oxidant property. Our data support this, suggesting that the presence of a high concentration of hypotaurine in the seminal fluid is important for the maintenance of the spermatozoa and secondarily supplements the production of hypotaurine by the fallopian tube to provide a favourable environment for fertilization of the ova.

The decrease in hypotaurine production after castration suggests either a decreased supply of cysteine or else a decrease in the activity and/or production of the enzyme for conversion of cysteine to hypotaurine. The latter seems to be the more likely possibility since both half-cystine (questionable in prostate) and methionine in the tissue pools were increased after castration and restored to or towards normal by testosterone.

In contrast to the accessory sex organs, the mouse kidney, a tissue highly responsive to androgens, contained only trace

Table 1 Effect of Testosterone on Hypotaurine, Taurine, Half-Cystine and Methionine Concentration in the Seminal Vesicle and Prostate of the Guinea-pig

Amino-acid	Normal (N) µmol g^{-1} ± s.e.	Castrate (C) µmol g^{-1} ± s.e.	%	Testosterone (T) µmol g^{-1} ± s.e.	%	N *vs* C *P*
		Seminal vesicles				
Hypotaurine	6.30±0.68	1.77±0.11	−72	5.73±0.33	−9	0.01
Taurine	5.98±0.30	6.49±0.26	+8	5.85±0.46	−2	0.3–0.2
1/2 Cystine	0.04±0.01	0.12±0.01	+236	0.07±0.02	+86	0.01
Methionine	0.26±0.02	0.48±0.02	+88	0.27±0.02	+4	0.01
		Prostates				
Hypotaurine	4.63±0.41	0.71±0.08	−85	3.48±0.33	−25	0.01
Taurine	4.64±0.39	5.64±0.13	+22	4.32±0.23	−7	0.05–0.02
1/2 Cystine	0.27±0.07	0.38±0.06	+38	0.43±0.05	+58	0.3–0.2
Methionine	0.37±0.04	0.70±0.02	+90	0.39±0.04	+5	0.01

There were 10 normal, 28 castrated and 20 testosterone treated guinea-pigs. The mean weights of the seminal vesicles were: N=762, C=241, T=754 mg and of the prostates were: N=585, C=258, T=508 mg. Each amino-acid analysis represents 2 normal, 4 castrated and 2 testosterone treated animals except that one of the treated samples was the pool from 10 guinea-pigs. The values represent the means of 5, 7 and 6 analyses for the respective groups.

quantities of hypotaurine but a greater concentration, two to three times that of the guinea-pig tissue, of taurine which was increased after castration and restored to normal by androgen treatment (unpublished).

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Morphological and Biochemical Alterations in Foetal Rat Brain Cells cultured in the Presence of Monobutyryl Cyclic AMP

I HAVE found that several aspects of the morphology and biochemistry of cultured foetal rat brain cells can be altered by N-monobutyryl-cyclic $3',5'$ monophosphate (N-but cyclic AMP). Dispersed cell cultures of foetal rat brain were grown for 15 days in the presence of 10^{-3} M N-but cyclic AMP and compared with similar untreated cultures. N-but cyclic AMP, prepared from dibutyryl cyclic AMP (Sigma) as previously described[1], was used because of its expected greater activity than cyclic AMP in an intact cell preparation[2]. It is more stable than the dibutyryl form which may release appreciable quantities of butyric acid[1].

Within 72 h after the addition of N-but cyclic AMP to cultures, cell division (as measured by protein accumulation) slowed, and the morphology of many cells had changed markedly. Multiple cell processes were elaborated, sometimes in a network (Fig. 1*A–D*). These cells comprised 25–50% of discernible cellular elements after 18 days in culture. They stained poorly with silver (Bodian technique) and were not electrically excitable when stimulated with intracellular electrodes. When N-but cyclic AMP was added to confluent cultures (10 days after plating), processes could still be formed (Fig. 1*E* and *F*). The effect on process formation could not be reproduced by inhibiting cell divi-

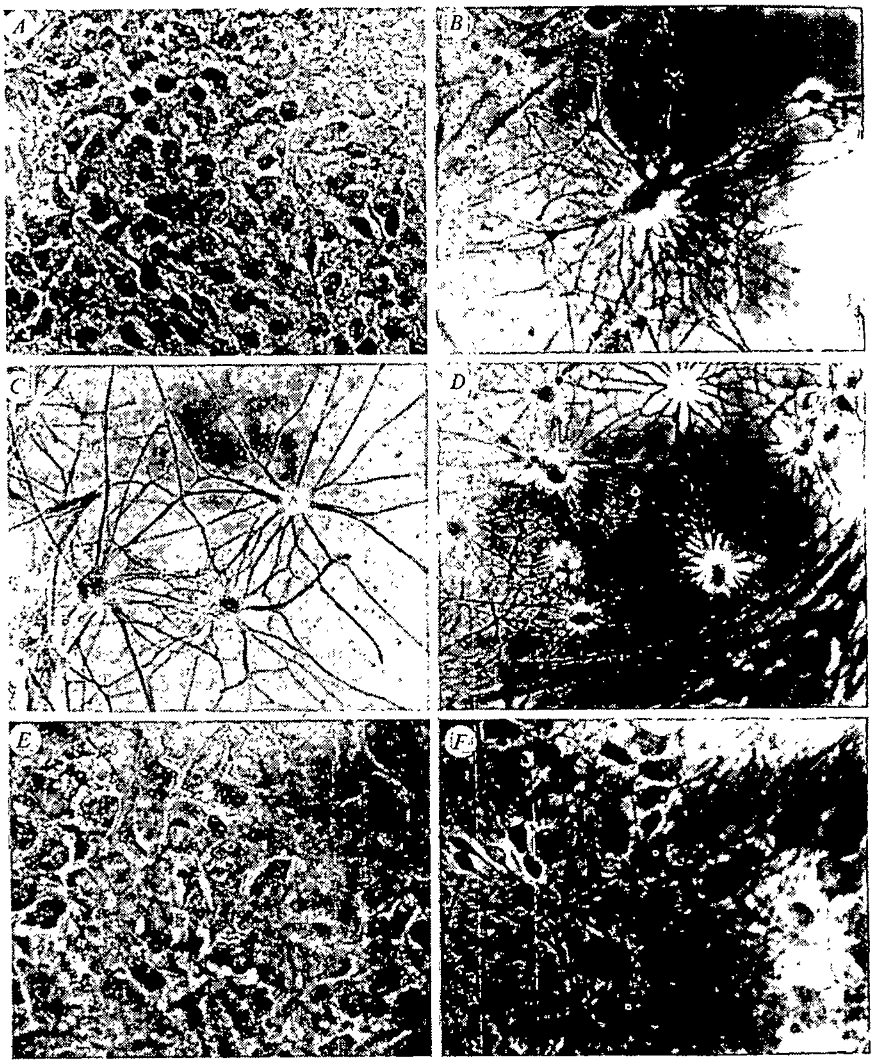

Fig. 1 Whole brains were obtained from foetuses of 18–21 day pregnant Fisher strain rats (NIH), dissociated in isotonic solution D[3] into single cells by passage through 210 µm and then 130 µm nylon cloth (Nitex; Tabler, Ernst, and Traber, Elmstord, New York), inoculated into polystyrene culture dishes (Falcon) at a density of 10^5 cells/cm^2, and grown in Dulbecco's modified Eagle's medium (GIBCO) containing 10% (v/v) foetal bovine serum (Colorado Serum Co., Denver), 10 U/ml. Na-penicillin G, and 10 µg/ml. streptomycin sulphate. Cultures were incubated at 37° C, 100% humidity, in an atmosphere of 10% CO_2–90% air. Medium (8 ml./dish) was changed on day 3 after plating and on alternate days thereafter; N-but cyclic AMP was first added on day 3 and subsequently at each medium change. The pictures are phase contrast micrographs (×135). *A*, Normal culture, 10 days; *B–D*, cultures treated with N-but cyclic AMP beginning day 3, 10 days; *E*, normal culture, 14 days; *F*, culture treated with N-but cyclic AMP beginning on day 10, 14 days.

sion with 5-fluorodeoxyuridine. Cultures treated with N-but cyclic AMP never achieved confluence and differed markedly from control cultures in their amount of protein (Table 1). This limitation of cell division was not accompanied by microscopic changes indicative of cell injury or death.

There were also substantial differences in the activities of the neurotransmitter-related enzymes acetylcholinesterase (acetylcholine acetylhydrolase; EC3117) and choline acetyltransferase (EC2136) (Table 1). In cultures treated with N-but cyclic AMP, acetylcholinesterase specific activity was 300% of the control value; choline acetyltransferase was 48% of the control value. These ratios were achieved by the twelfth day of culture and remained stable until day 18. Cyclic AMP has previously been reported to increase acetylcholinesterase in cultured neuroblastoma cells[7], and to increase both acetylcholinesterase and choline acetyltransferase in cultures of foetal chick brain[8].

Table 1 Protein and Enzyme Activities after 18 Days in Culture

	Control	+N-but cyclic AMP
Protein (mg)/culture	1.890	0.392
Choline acetyltransferase, pmol*	83	40
Acetylcholinesterase, nmol*	2.15	6.45

* Product formed/min/mg protein.

Methods for preparation of cells for assay[4] and determination of acetylcholinesterase[3], choline acetyltransferase[3], and protein[5] have been previously reported. Acetylcholinesterase specificity was verified with Burroughs Wellcome compound 284C51 (1,5-*bis*-(allydimethyl-ammoniumphenyl)pentane-1,3-dibromide), 10^{-5} M (ref. 6). The radioactive product of the choline acetyltransferase assay was determined to be >95% acetylcholine by paper chromatography as previously described[4].

The identity of the process-forming cells could not be determined with certainty. The lack of increase in the activity of choline acetyltransferase, a putative neuronal enzyme, and the electrophysiological and histochemical evidence indicated that they were probably not neurones. Besides neurones and glial cells, a few endothelial, ependymal, and fibroblast-like cells were probably present in the cultures, but the abundance and appearance of the cells with processes suggested that they were of glial origin.

Cyclic AMP (or one of its analogues) can affect cell division[9,10] and morphology[2,11] in tumour cells and permanent cell lines. My results show that it markedly affects these properties in primary cultures of cells from the developing rat brain. Enzyme activities were also affected, but it is not known whether the changes resulted from selective growth effects or alterations in gene expression. Mechanisms mediated by cyclic AMP may play a role in mammalian central nervous system development.

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Relationship between Protein Synthesis and RNA Content in Skeletal Muscle

EXTENDING our studies on the adaptation of muscle synthesis to dietary stress[1,2], we investigate here the relationship between concentrations of tissue RNA and rates of protein synthesis. Dietary regimes which depress protein synthesis also lead to a fall in tissue RNA content[3,4]. This fall may reflect a reduced need for cellular RNA components, or it may itself be of primary importance in determining the rate of protein synthesis. More than 80% of muscle RNA is ribosomal and this proportion appears to be maintained during protein depletion[5], so that a change in RNA also reflects a change in ribosome content. If alteration in ribosomal content effects control, then this alteration may be termed a change in the ribosomal capacity for protein synthesis. If, however, a change in synthesis is brought about by alterations in the other factors modulating each phase of translation, then it is a change in the ribosomal efficiency. This will be demonstrable as alterations in the amount of protein synthesized per unit RNA. We have investigated the extent to which alterations in rates of protein synthesis result from changes in the capacity for and the efficiency of protein synthesis in muscle.

We have measured the rate of muscle protein synthesis *in vivo* by means of the constant intravenous infusion technique[7]. Rats were infused *via* the tail vein with trace amounts of ^{14}C tyrosine for 6 h; the plasma and intracellular specific radioactivities in tyrosine quickly rise to a plateau, and the rate of protein synthesis was calculated from a single measurement of the specific radioactivity of the free and protein-bound tyrosine at the end of the infusion[8]. Measurements of the rate of protein synthesis and muscle RNA content were made on rats which had been starved, or fed either a standard protein (net dietary protein energy ratio 10%) or a protein free diet. Groups of animals were also fed the 10% diet after 3 weeks of the protein free regime.

Table 1 shows that muscle synthetic rates fell markedly on the dietary regimes which involved starvation or a protein free diet. Refeeding with the 10% diet, after 21 days lacking protein, led to a prompt increase in the rate of protein synthesis but the rates were still less than those in the control group.

Starvation or protein free feeding led to a decline in the RNA concentration, expressed as the RNA to protein ratio, and this was partially restored by refeeding the 10% diet. The rate of protein synthesis per unit RNA (the efficiency of protein synthesis) was calculated from the data in the first two columns of Table 1. Despite considerable variations in the rates of synthesis the animals could be separated into two groups. Group *A*, with an average efficiency of 14.0 μg protein synthesized μg RNA day^{-1}, included all the rats receiving protein in their diet. The remaining animals, Group *B*, were starved or fed the protein free diet and displayed a reduced efficiency with an average of 9.3 μg protein synthesized/μg RNA/day.

The relationship between the rate of synthesis and the RNA concentration for the individual animals in each of the two groups is shown graphically in Fig. 1. Wide variation within the two groups in RNA concentration is correlated with similar changes in the rate of protein synthesis. These variations therefore reflect changes in the capacity for protein synthesis, whereas a transition between the two groups reflects a change in the efficiency of synthesis.

When the time course of the changes is considered, it is clear from Table 1 that the short term responses of muscle protein synthesis to dietary changes predominantly reflect changes in efficiency of synthesis. The change to a new level of efficiency occurred within 24 h of fasting or feeding the protein free diet, and this change was readily reversible when dietary protein was restored. Such abrupt changes in efficiency as those found with our dietary regimes might not have been so large if graded reductions in the protein content of the diet had been tested. The subsequent changes in protein synthesis were a result of alterations in the capacity, which fell progressively throughout the first 10 days on the protein free regime and then gradually increased with refeeding. The changes in capacity were not as rapid as those in efficiency, but were of equal quantitative importance by the second day of protein free diet and after 10 days were responsible for the major part of the reduction in muscle protein synthesis.

These investigations are similar in some respects to those reported by Henshaw *et al.*[9], who measured synthesis rates *in vivo* in small numbers of fasting and fed rats by a single injection of large amounts of ^{14}C lysine. The efficiency of synthesis in their fasted rats fell to between one half and one quarter of the efficiency in their fed animals, but within the fed group their measurements of efficiency varied from values equivalent to 2.2 to 7.7 µg protein/µg RNA/day. Because of this variability and the higher efficiencies in our animals no strict comparison between results is possible. Large variations in rates of protein synthesis may occur over 20 min intervals, as measured by Henshaw *et al.*, but these fluctuations would be of little quantitative importance in determining muscle protein mass unless the synthetic rates were sustained for sufficiently long to become apparent with a 6 h infusion. The synthetic rates presented here agree closely with measurements using tracer infusions of glycine[10] and lysine[6] and with those values calculated from the decay of ^{14}C carboxyl labelled aspartate and glutamate in muscle protein[11]. This latter technique makes no assumption about the specific activity of the precursor for protein synthesis.

Most of the information about the control of protein synthesis comes from *in vitro* experiments, many of them involving purified or semi-purified components. It is very difficult to extrapolate directly from measurements *in vitro* to the condition *in vivo*. For example most *in vitro* studies of muscle protein synthesis involve systems in which no initiation occurs, limiting the study to mechanisms of elongation and termination[12,13], and precluding the quantitative assessment of the importance of any single factor in the intact process *in vivo*. Lack of initiation is one reason why rates of protein synthesis *in vitro* are often much slower than *in vivo*[9]. Our studies demonstrate that while changes in the efficiency of protein synthesis do occur *in vivo* and are important in initiating short term changes in protein synthesis, the changes produced by a longer exposure to dietary stress seem to result from an alteration in the capacity for protein synthesis; that is a loss of the RNA components of the translational apparatus.

Table 1 Effect of Diet on the Rate of Muscle Protein Synthesis and RNA Content of Rat Skeletal Muscle

Diet		*n*	Synthesis rate (ks day^{-1})	RNA (µg RNA/ mg protein)	Synthesis/ RNA µg protein/ µg RNA/day
Stock	Control	9	0.153 (0.031)	11.53 (1.01)	13.1 (2.5)
	1 day refed	6	0.070 (0.013)	4.91 (0.57)	14.4 (3.0)
	2 days refed	4	0.080 (0.020)	5.44 (0.56)	15.5 (4.0)
	3 days refed	4	0.095 (0.020)	7.35 (0.88)	14.0 (2.5)
A		23			14.0 (2.86)[1]
Protein free	1 day	6	0.098 (0.011)	10.50 (0.57)	9.3 (0.8)
	2 days	5	0.083 (0.005)	8.37 (0.53)	9.8 (0.6)
	10 days	4	0.052 (0.009)	4.78 (0.67)	10.3 (1.6)
	21 days	5	0.043 (0.006)	4.78 (0.23)	9.1 (1.5)
Fasted	1 day	6	0.087 (0.007)	9.59 (1.01)	9.2 (1.3)
	2 day	3	0.070 (0.009)	8.71 (0.79)	7.8 (0.5)
B	29				9.3 (1.24)[1]

Significance between numbered groups $1 = P < 0.001$.

100 g male albino rats were infused *via* the tail vein with ^{14}C tyrosine (s.a. 10 mCi mmol^{-1}) in normal saline (2 µCi ml.$^{-1}$) at a rate of 0.5 ml.$^{-1}$ h for 6 h. The rats were then decapitated and the quadriceps and gastrocnemius muscles excised and homogenized in ice-cold 10% TCA. Specific radioactivity of free and protein-bound tyrosine was measured and the rate of protein synthesis calculated[8]. The RNA and protein content were measured[14]. Results are shown as mean ± s.d.

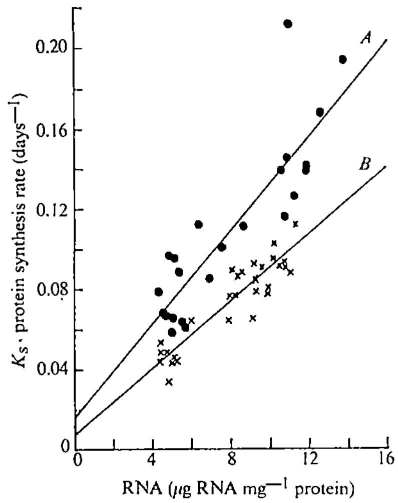

Fig. 1 Relationship between rates of protein synthesis and RNA concentrations in rat skeletal muscle. Results are the individual results shown as means of groups in Table 1. The regression analyses were performed separately on groups *A* and *B*. The lines correspond to equations

$$K_s = 0.0117 \frac{\text{RNA}}{\text{protein}} + 0.016 \text{ (group } A) \quad r = 0.874$$

$$\text{and } K_s = 0.0084 \frac{\text{RNA}}{\text{protein}} + 0.0070 \text{ (group } B) \; r = 0.909$$

The gradients of the regression lines are significantly different at the level $0.05 > P > 0.02$.

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Basilar Membrane Correlates of the Combination Tone $2f_1$–f_2

GOLDSTEIN[1] has shown that when two tones of frequency f_1 and f_2 ($f_2 > f_1$) are heard simultaneously, the most prominent distortion product is the combination tone of frequency $2f_1—f_2$. It is observed most strongly when the ratio $f_2/f_1 = 1.1$, when it is typically only 15 dB below the level of the primary tones. The relative amplitude can be measured by cancellation and is substantially independent of input level, that is, it can be considered as an essential non-linearity, but it decreases rapidly as the ratio f_2/f_1 is increased. These features seem to rule out Helmholtz's[2] explanation based on simple limiting distortion in the middle ear.

Goldstein and Kiang[3] extended the psychophysical findings by studying single auditory nerve fibres in cat. They found that under suitable conditions fibres would respond to f_1 and f_2 together but to neither alone. Also, fibres of low characteristic frequency responded in a phase locked manner to $2f_1—f_2$ and could be desynchronized by adding a real frequency component at $2f_1—f_2$ of appropriate amplitude and phase.

These results suggested that the combination tone $2f_1—f_2$ was generated within the cochlea and might be present as a vibration of the basilar membrane. The necessity for two frequency filters, one before the essential nonlinearity and the other following it, was appreciated by both Goldstein[1,4] and Smoorenburg[5]. The essential nonlinearity was either in the hydrodynamics of the cochlea[6] or in the hair cell motion. It was assumed that the distortion products were coupled back to the basilar membrane and analysed at their proper place by the second filter. Here we tested some of these assumptions by measuring the mechanical vibration component at $2f_1—f_2$ on the basilar membrane in guinea-pig.

Measurements of basilar membrane vibration were made with a miniature capacitive probe with a tip diameter of 0.15 mm (J. P. W., manuscript in preparation), utilizing the same principle as Békésy[7]. Amplitudes down to 1 Å were measured using a phase sensitive amplifier. The probe was attached to a moving armature system which was used both for the fine adjustments of the probe-membrane distance and also for calibration of the system by vibration of the probe through a known distance.

The guinea-pigs were 300–500 g, and were anaesthetized with pentobarbitone sodium and fixed in a stereotaxic frame with hollow ear bars. They were paralysed with gallamine triethiodide and artificially respired. The cochlea was exposed by opening the bulla, the first turn opened and the perilymph drained from scala tympani. The probe was placed about 20 µm from the surface of the basilar membrane.

Sound was presented closed field from a 'Bruel and Kjaer 4134 microphone' and calibrated with a 1 mm probe tube microphone. The frequency response of the basilar membrane was first measured and plotted automatically from 20 Hz to 20 kHz using the capacitive probe and a 'Bruel and Kjaer 1024' oscillator, '2020 Heterodyne Slave Filter' (3.16 Hz bandwidth) and '2305 Level Recorder'. A 'Brookdeal 401 Lock-In Amplifier' was used for measurements up to 50 kHz and for combination tone measurements. When the frequency giving maximal vibration for a constant SPL input had been established, frequencies f_1 and f_2 were chosen so that $2f_1—f_2$, f_1 and f_2 were in this region and so that the ratio f_2/f_1 was close to 1.1. The vibration at $2f_1—f_2$ was determined from the in-phase and quadrature components on the lock-in amplifier. The synchronizing signal required for the amplifier was generated by a diode mixing circuit and filtered using the 'Bruel and Kjaer 2020 filter'. Care was taken to avoid drift of phase during the measurements.

Threshold for N_1 response to clicks was measured regularly on the bony cochlea and increased systematically throughout the experiment. Opening the first turn and draining the perilymph had no direct effect on threshold, which increased by less than 3 dB.

The frequency response and peak amplitude of the basilar membrane vibration were found[8] to be similar to those reported by Johnstone, Taylor and Boyle[9]. Although the levels of vibration at $2f_1—f_2$ were measured absolutely they were converted to equivalent levels of sound input and expressed relative to the average level of the primaries (Table 1).

Table 1 $2f_1—f_2$ Component of Basilar Membrane Vibration* for Various Combinations of Frequency and Level of the Primary Tones

Animal	Peak of BM response (kHz)	$2f_1-f_2$ (kHz)	f_1 (kHz)	f_2 (kHz)	SPL of f_1 (dB)	SPL of f_2 (dB)	Average level* of $2f_1-f_2$ relative to primaries (dB)
142L	21	18	20	22	112	111	−41
		20	22	24	111	110	−45
149L	20	16	18	20	101	101	−55
		16	18	20	111	111	−37
		20	22	24	100	99	<−60
		20	22	24	110	109	−54
153L	21	18	20	22	89	90	<−51
		18	20	22	99	100	−52
		20	22	24	90	94	−55
156R	23	20	22	24	103	102	<−50
		20	22	24	113	112	−41

* Expressed as the sound input which would have been required to give the observed level of vibration at $2f_1—f_2$.

Instrumental distortion including the sound generator was less than −60 dB so the figures represent distortion within the animal. At the lower levels measurement was generally limited by the noise level of the capacitive probe. The higher level of distortion at the higher SPLs is consistent with overloading distortion rather than an essential non-linearity.

In experiments at 90 and 100 dB SPL the level of $2f_1—f_2$ reached 55 dB below the primaries, about 40 dB below the level required to account for the psychophysical and neurophysiological results.

We have failed to find any significant component of basilar membrane vibration of frequency $2f_1—f_2$ in the first turn at 90 and 100 dB SPL. This result seems to conflict with the kind of model described earlier. There are other, less likely explanations for our results which do not conflict. (1) Our operative procedure may disturb the mechanism of the cochlea. This is unlikely as Evans[10] has shown that the tuning curves of single cochlear nerve fibres in guinea-pig are unaffected by a similar procedure, and we verified that click threshold is substantially unaffected by opening and draining the first turn. Also, although measurements were never complete before the N_1 threshold had risen by 15 dB, there was no evidence that any of the mechanical parameters varied even for large changes in N_1 threshold. (2) There may be a species difference. The combination tone $2f_1—f_2$ has been demonstrated only in man (psychophysically) and cat (neurophysiologically). No other qualitative differences of structure or function have been found, however, and there is no reason to believe one exists for this phenomenon. (3) The combination tone $2f_1—f_2$ may not be present at the high frequencies necessary for measurements in the first turn. Goldstein[1], however, showed it to be little affected by frequency range, Goldstein and Kiang[3] suggest that it is present throughout the audible range, and a response was observed to $2f_1—f_2$ at 27.5 kHz in a cell in cat cochlear nucleus (J. P. W. and E. F. Evans, unpublished data). (4) The sound intensities used may have been too high. Although overloading distortion increases with level there is some evidence that the proportion of $2f_1—f_2$ decreases slightly at higher levels, but this was not a great decrease. Goldstein[1] found the effect of increasing the primaries from 30 to 70 dB SL was only 2 to 6 dB, and Zwicker's[11] cancellation level for $f_1 = 1$ kHz, $f_2 = 1.3$ kHz at 80 and 90 db SPL agrees with Goldstein's value at 50 dB SL and was about 10 dB less at 100 dB SPL. The synchrony of nerve fibre respose up to 100 dB SPL was found to be not strongly dependent upon stimulus level[3].

Reconsidering models which involve pre-filtering, essential non-linearity and post-filtering, some modifications appear to be essential. First, the non-linearity cannot be hydrodynamic[6] but may be in the coupling between basilar membrane and excitation of hair cells. Dallos[12], however, has shown that $2f_1-f_2$ in cochlear microphonics does not vary appropriately with f_2/f_1 and sound level. Assuming that $2f_1-f_2$ is present mechanically he concluded that the microphonic potential might not be an essential link in the peripheral transduction process. Our results make this conclusion unnecessary; cochlear microphonics do reflect the receptor potentials; the non-linearity would be central to the receptor potentials. Second, the second filter cannot be closely coupled to the basilar membrane but its location and nature have not yet been identified. Like the non-linearity, it presumably comes after the mechanical transduction process but must precede the generation of nerve impulses.

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Pituitary Inhibition of Pregnancy

HERE I report some new and unexpected findings on the role of the pituitary in the reproductive cycle of the tammar wallaby, *Macropus eugenii*. My results suggest a pituitary suppression of the corpus luteum during the seasonal embryonic diapause found in this species. They may have some relevance to the hormonal control of the analogous seasonal delayed implantation of eutherian species such as the badger, *Meles meles*[1]; the roe deer, *Capreolus capreolus*[2]; and the black bear, *Ursus americanus*[3].

The female tammar wallaby usually produces one young in January or early February. Mating occurs at a post partum oestrus, and the resulting blastocyst remains quiescent in the uterus and the corresponding corpus luteum is quiescent in the ovary until the next year[4]. The young suckles in the mother's pouch for up to 8 months and during this time the female remains in lactational anoestrus. Removal or loss of the pouch young during the breeding season causes resumption of development of the quiescent corpus luteum and embryo and a new young is born 27 days later. The wallaby does not breed between June and December, however, and removal of the pouch young during this seasonal anoestrus has no effect on the quiescent corpus luteum or embryo. They remain in "embryonic diapause"[5] until the following breeding season, when they resume development presumably in response to environmental stimuli[6].

I have developed methods of hypophysectomy[6] and radioimmunoassay for gonadotrophin[7] to examine the influence of the pituitary on reproduction in wallabies which is suggested by these phenomena. The results obtained do not conform to the conventional concepts of pituitary activity in reproduction.

Groups of three wallabies were hypophysectomized at four-day intervals through pregnancy after removal of pouch young. Pregnancy continued, although hypophysectomy on the fourth day retarded embryonic growth, and the cycle of the corpus luteum of pregnancy also proceeded normally. Hypophysectomized animals, however, did not give birth; at autopsy they had dead full-term embryos in their uteri. Ovarian follicular growth and oestrous changes were suspended. In contrast, sham hypophysectomized control animals gave birth on the expected date and had a normal post partum oestrus and ovulation. Correspondingly, radioimmunoassay of peripheral plasma, taken daily after removal of pouch young from six intact wallabies through pregnancy and post partum oestrus, showed peaks of plasma gonadotrophin (11–18 ng ml.$^{-1}$) coincident with oestrus, but basal levels (2–5 ng ml.$^{-1}$) throughout pregnancy. The pituitary therefore was not essential for any stage of the pregnancy that followed removal of pouch young.

A group of wallabies was hypophysectomized before removal of pouch young (during lactational anoestrus). Lactation ceased within two days, although young remained on the teats for a further two to five days. The quiescent corpora lutea and blastocysts of these animals resumed development and pregnancy went to term. This suggested that resumption of embryonic development was independent of pituitary stimulus, but might be governed by lactation inhibition during the breeding season. To test this, six lactating wallabies were hypophysectomized in the non-breeding season. Lactation again ceased within two days, and the quiescent corpora lutea and blastocysts resumed development. Sham hypophysectomized controls showed no development. It seemed that the corpus luteum or blastocyst was being suppressed either by the mammary gland or by the pituitary. Seven non-lactating wallabies were therefore hypophysectomized in the non-breeding season. Corpora lutea and embryos again resumed development. Inhibition was evidently due either directly or indirectly to the pituitary.

The influence of the mammalian pituitary gland in pregnancy has been studied in about twelve eutherian species[8]. In all except the guinea-pig, *Cavia porcellus*[9], hypophysectomy before implantation caused death of the embryo. Most species were intolerant of the operation before the second half of pregnancy, while in the dog, *Canis canis*, and rabbit, *Oryctolagus cuniculus*, embryos died when hypophysectomy was performed at any stage[8]. The guinea-pig is unique among eutherian species studied in that the corpus luteum of pregnancy continued to grow after hypophysectomy[9]; in others it degenerated. The effect of complete hypophysectomy on the parturition of eutherians is not clear, but several species are reported to have produced live young when hypophysectomized late in pregnancy[8]. Termination of lactation, follicular growth and normal cyclical oestrus after hypophysectomy are general among the eutherian species that have been studied, and the hypophysectomized wallaby is no exception in this.

The unexpected resumption of embryonic development in non-lactating wallabies hypophysectomized in the non-breeding season suggests a pituitary inhibition of the corpus luteum. If so, embryonic diapause in the normal wallaby is presumably ended by removal of a pituitary inhibition, and not by gonadotrophic action. A similar mechanism may be involved in delayed implantation of eutherian species. A pituitary inhibition of embryonic development during delayed implantation in badgers would explain why even massive injections of gonadotrophins fail to terminate delayed implantation in that species[1]. The inhibitory role may be played by oxytocin, as workers on eutherian species have demonstrated partial or total inhibition of the corpus luteum by oxytocin[10-11], and oxytocin inhibits development of the corpus luteum of red kangaroos after removal of pouch young[12].

Photoperiod is probably an important controlling factor. The delayed blastocyst of the badger will implant under experimentally reversed photic and climatic conditions[13] and the tammar wallaby reverses its breeding season when translocated to the northern hemisphere[14].

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The Expression of Female Sex-limited Characters in the Male

DESPITE very different reproductive characteristics of males and females, autosomal genes controlling these characters are common to both sexes. (The transmission of genes for female fertility through the males is demonstrated by differences in the reproductive performance of the daughters of different sires[1,2].) Furthermore, the fact that the same gonadotrophic hormones are intermediaries in the physiological control of reproductive activity in both sexes is well established[3]. The quantitative expression of sexual activity in males and females may therefore be genetically correlated, a possibility which is supported by the observation that breed and seasonal differences in ovine female fertility are associated with differences in male libido[4].

In view of the limitations to the selection differential which can be applied to sex limited characters such as fertility, potential relationships between male and female reproductive activity were investigated in two species, the mouse and the sheep. In the mouse study, the testis weight of male mice was examined in lines in which the ovulation rate had been changed following twelve generations of direct selection for natural or induced ovulation rate[1]; and in the sheep work, the growth of the testis was examined in two breeds, the Finnish Landrace and the Tasmanian Merino, which have more than a three-fold difference in litter size[5], and in the cross between them.

The males of the last selected generation of the four mouse strains, and the control, were killed at approximately 10 weeks of age, and their testes removed and weighed. The mean testis weight of the control and four selected lines was then expressed as the mean of the 16 family means which made up that line, in the same way that the mean of family means was used to measure body weight and ovulation rate. These mean testis weights are given in Table 1 together with the body weights of these individuals at the time of slaughter and the natural ovulation rate of their primiparous female contemporaries. Body weight and testis weight are seen to have changed in the same direction as the ovulation rate, the divergence of testis weight between the lines selected for both high and low natural and high and low induced ovulation rate being statistically significant ($P<0.05$). The relationships between body weight and ovulation rate have been described earlier[6].

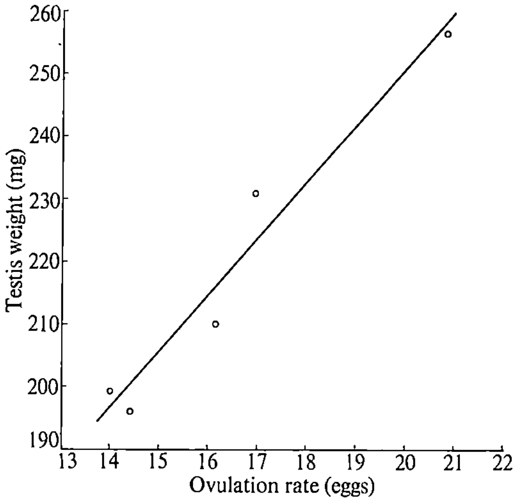

Fig. 1 Relationship between mean testis weight and mean ovulation rate of five mouse lines selected for ovulation rate. The between line regression of testis weight on ovulation rate was: testis wt. (mg) = 70 + 9 × ovulation rate.

The change in testis weight following selection for ovulation rate indicates that the expression of the two traits may be genetically correlated and this relationship is illustrated in Fig. 1 as the mean testis weight of the lines plotted against their mean natural ovulation rate. The correlation between them is 0.97 and the genetic regression of testis weight on ovulation rate as estimated from the observed divergence of the high and low natural lines, 8.4 mg per egg. Although part of the change in testis weight may have arisen from changes in body weight, the partial correlation between ovulation rate and testis weight for constant body weight was 0.82, indicating that the removal of variation in body weight had only a small effect on the magnitude of the correlation between ovulation rate and testis weight. This indicates that ovulation rate and testis weight are genetically correlated in the mouse population

Table 1 Mean Ovulation Rates and Testis Weights of Selected Mouse Lines

Line	Body weight (g) (C. 10 wks)	Ovulation rate	Testis weight (mg)
High natural	34.72±3.66	20.87±0.54	257±22.0
Low natural	29.68±1.18	13.98±0.54	199±22.1
High induced	31.48±2.61	16.84±0.73	231±23.2
Low induced	27.37±2.12	14.41±0.50	196±21.6
Control	31.27±1.66	16.13±0.45	210±19.1

studied and that this correlation is not solely mediated through body weight; the magnitude of the genetic correlation is, however, dependent upon several factors, including the heritability of testis weight for which no estimates are available.

The growth rate of the testes of the sheep was examined in terms of the testis diameter of pure and crossbred males, measured at weekly intervals from 8 to 26 weeks of age over the period of rapid growth[7]. The testis diameter of ten Finn, four Merino and nine crossbred males was measured as the difference between the thickness of a fold of scrotal skin and the overall diameter of the testis and two layers of skin. The $\log_e$ mean weekly testis diameter is plotted against the $\log_e$ mean weekly body weight in Fig. 2; the regression coefficients are 2.16 mm kg^{-1} for the Finnish Landrace males, 2.65 for the crossbreds, and 2.27 for the Tasmanian Merino males, the crossbred regression coefficient being significantly greater ($P < 0.05$) than that of the pure breds. The growth rate of the testes was therefore similar in the two pure breds, but their mean diameters were significantly different—that of the Finnish Landraces exceeding that of the Merinos throughout the study. As the testes of the crossbred males grew faster in diameter than those of the parental breeds, they showed heterosis in this character such that at $\log_e$ body weight = 3.2 they exceeded those of the larger parent.

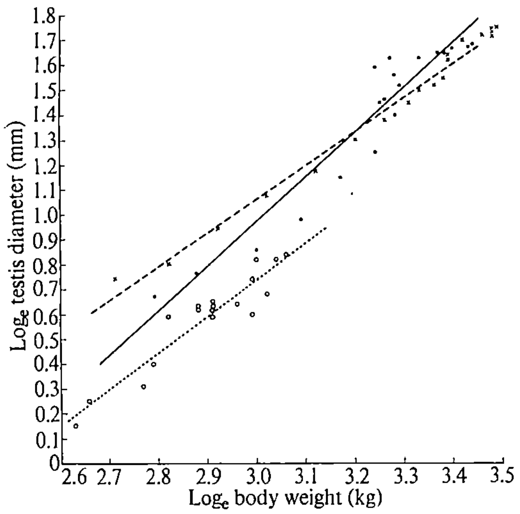

Fig. 2 Increase in testis diameter relative to body weight in Finnish Landrace (× --- ×), Tasmanian Merino (O . . . O) and Merino (♂) cross Finn males (◑ --- ●) from 8 to 26 weeks of age.

In both sheep and mice, testis weight or diameter was greater in the line or breed with the higher ovulation rate, indicating that the quantitative expression of reproductive characteristics in male and female mammals is genetically correlated. This correlation may, of course, be mediated *via* one or more of several physiological systems, and although the present experiments do not help to differentiate among these, between breed studies (refs. 8 and 9 and Land, Pelletier, Thimonier, and Mauléon, in preparation) of pituitary and plasma gonadotrophin activity have indicated that differences in sheep fertility may be related to differences in LH activity. Regardless of the physiological pathway underlying the genetic correlation, this correlation indicates that it might be possible to base genetic selection for increased fertility—or some measures of fertility—in the female on the reproductive characteristics of the male. More generally, measures of fertility in either sex may not be wholly sex limited.

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IQ Evoked Responses and Fourier Analysis

CONFLICTING results have been obtained in studies[1–3] dealing with Fourier analysis of evoked responses (ER) in relation to human intelligence. On rethinking, I realized (*a*) that the spectral characteristics of ER change with time, and (*b*) that most of the differences between high and low IQ subjects appear to occur in the first 150 ms of the response.

Previously Fourier analyses looked at a 0.5 s slice of ER which does not take into account its non-stationary properties. I have, therefore, applied a technique used in speech recognition[4,5] in which Fourier analysis is performed in a sliding time window. Zero padding is used to improve definition of the spectral peaks[6,7].

From an FM tape library of over 1,000 subjects, I selected a high and a low IQ group on the following basis: IQ scores of 120 plus on two out of three IQ tests given—the Otis, PMA and WISC yielding 92 high IQ subjects. The low IQ group had IQs of 85 or less on two out of the three tests yielding 71 subjects. The total sample of 164 represents all subjects available to me who met these criteria. The mean age of the subjects was 11.6 years, with a range of 7.5 to 15.3 years. Of the total, ninety-two were males and seventy-two were females. All of these subjects were from the school population and all have had routine medical examinations; none of the subjects had diagnosed organic illness of any sort.

Data on FM tapes were as follows. The EEG was derived from bipolar scalp contact electrodes 6 cm apart astride C_4 in the 10–20 system. The EEG was recorded in a bandwidth 3 dB down at 3 and 50 Hz with an attenuation slope of 24 dB per octave. Four hundred trigger pulses corresponding to the onset of photic stimuli were also recorded. The data were converted to digital form (250 Hz sampling rate, 6 bit amplitude quantization) and a conventional amplitude average was computed over 400 stimuli using the first 60 sample points representing 240 ms of record. Fourier analysis was then performed in an 80 ms time window which was incremented in 8 ms steps from 40–200 ms. Frequency definition was 1 Hz (using zero padding) from 12–50 Hz. The average amplitude of the Fourier transform of the high and low IQ subjects was computed for each time increment and at each frequency in steps of 1 Hz from 12–50 Hz resulting in a two-dimensional matrix of Fourier amplitude coefficients with time and frequency as the independent variables.

The coefficient matrices for subjects in the high and low IQ groups have been averaged over each group. For each cell, t-tests were computed for the frequency *versus* time shift matrix of high and low IQ subjects. A coherent and statistically significant band of t values was obtained indicating that the group of high IQ subjects have significantly more energy content in the frequency band of 18–29 Hz at 88 to 136 ms following the stimulus (Table 1). It is interesting to note that

Table 1 Frequency and Time Shift where High IQ Subjects Have Significantly ($P\geq 0.05$) Greater Energy Content in Their Fourier Transform Than Low IQ Subjects

Frequency (Hz)	Window centre position (ms)
12	136, 176
13	136, 176
14	136, 176
15	136, 176
16	136, 176
17	136, 176
18	104, 128, 136
19	104, 128, 136
20	104, 112, 120, 128, 136
21	104, 112, 120, 128, 136
22	96, 104, 112, 120, 128
23	96, 104, 112, 120, 128
24	88, 96, 104, 112, 120, 128, 152
25	88, 96, 104, 112, 120, 128, 152
26	88, 96, 104, 112, 120, 128
27	88, 96, 112, 120
28	88, 96, 112, 120
29	88, 96, 112
30	88
31	88
32	88
33	— — —
34	— — —
35	— — —
36	— — —
37	160
38	152, 160
39	152, 160
40	152, 160
41	120
42	120
43	64
44	64, 176
45	64, 176
46	64, 96
47	64, 96
48	64, 96
49	56, 64
50	56, 64

Fourier analysis was done with an 80 ms time window incremented in 8 ms steps from 40–200 ms.

in all cells where significant t values were obtained, high IQ subjects always had more energy content than low IQ subjects.

Although many significant t values were obtained, it is difficult to classify individuals based on these mean differences. Therefore, this technique by itself is not useful clinically. It is, however, important to know the nature of the individual differences in the spectrum of ER. The use of Fourier analysis over long time windows is inappropriate when applied to non-stationary phenomena, such as the ER, and this may explain the conflicting results obtained by the previous authors cited.

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New Aspects of *Salmonella* Infection in Broiler Production

Poultry are a considerable reservoir of salmonellae and a common source of infection in human *Salmonella* epidemics[1]. In 1971 a severe outbreak of *Salmonella infantis* infection occurred among Finnish broiler flocks, and 277 human cases[2] were diagnosed as caused by the same serotype. The broiler industry suffered serious losses through confiscation of broiler meat and elimination of infected birds.

As broiler production is carried out under abnormally hygienic conditions we suspected that the prevalence of *Salmonella* infection in broilers as compared to layer hens was caused by a hampered development of the intestinal flora, which normally participates in defence against pathogenic bacteria.

We present here the preliminary results of experiments studying the way in which normal adult gut contents given to baby chicks affect their susceptibility to *S. infantis* infection. These chicks were compared to similar chicks in conditions simulating the normal broiler house. The test animals were offspring of Cornish cocks and Pilch de Kalb hens hatched in a commercial broiler hatchery. The egg shells were disinfected with formalin gas. At the age of 1–2 days, 26 chicks received 0.5 ml. of gut contents (ingesta) from adult cocks, diluted with physiological saline 1 : 10 (w/v). Ingesta were taken from the crop and intestinal tract of three healthy cocks and were placed directly in the chick crops. Another group of twenty-four chicks served as controls. The groups were reared separately and all the birds were held in isolation. One day after the first treatment, both groups were divided into two subgroups. One of the subgroups was given approximately 10^3 and the other 10^6 *S. infantis* isolated from a field case (Table 1) into the crop.

Feeding began immediately after introduction of *Salmonella*. The feed did not contain antibiotics, chemotherapeutics or coccidiostats. Chicks were killed when they were 8–22 days old, using ether inhalation. The same number of birds from each group were killed at the same time. A bacteriological examination was performed on the crop, the small intestine and the caeca (Tables 1 and 2).

All the birds in control groups C and D (Tables 1 and 2) remained *S. infantis* carriers. In groups A and B which received ingesta before infection, 77% of the group given the smaller inoculum and 69% given the larger were free from *S. infantis*.

Table 1 shows the numbers of *Salmonella*-positive samples and Table 2 the numbers of salmonellae. During the experiment one bird died in each of groups C and D, and were excluded from the tables. Both chicks had more than 10^6 salmonellae per g in the caecal contents.

These results clearly demonstrated the inhibitory effect of ingesta on the establishing of *S. infantis* in the broiler gut.

The large numbers of salmonellae (10^6–10^9 g^{-1}) found in the caeca of birds without pretreatment point to a possible preferential colonization in that part of the intestine. *S. infantis* has most often been found in caeca[5]. In those pretreated birds which had salmonellae, the numbers were very low. In birds without pretreatment the numbers of salmonellae recovered from the crop and small intestine showed great variation. The experiment was subsequently successfully repeated.

Table 1 Occurrence of *Salmonella infantis* in Contents of Crops, Small Intestines, and Caeca of Experimentally Infected Chickens

Group	Pretreatment of chickens 1–2 days old	Number of *S. infantis* given orally*	Number of chickens examined	Birds with salmonellae recovered from different sections of the digestive tract							
				Crop		Small intestine		Caeca		At least one sample positive	
				No.	%	No.	%	No.	%	No.	%
A	Pretreatment	10^3	13	2	16	1	8	0	0	3	23
B	Pretreatment	10^6	13	3	23	1	8	1	8	4	31
C	No pretreatment	10^3	12	7	58	7	58	12	100	12	100
D	No pretreatment	10^6	10	8	80	6	60	10	100	10	100

* Numbers of salmonellae given are approximate.

Grouping made according to pretreatment with contents of the digestive tract and doses of salmonellae.

Bromthymol blue-lactose-saccharose-agar, triple-sugar-agar and urea-agar were used as culture media. Selenite broth was used for enrichment. All the substrates were produced by Orion Pharmaceutical Co., Helsinki, Finland. The sera employed for typing were produced by Behringwerke AG, Marburglahn, Germany.

On the basis of these results we wish to put forward the hypothesis that as the development of the intestinal flora is delayed when broilers are produced in a *milieu* low in microbes, the newly hatched birds are in a transitional state between germ-free and normal animals for a few days. The defence against bacteria entering the body through the mucosa or colonizing on it is probably weaker than normal. This state is remedied by administering intestinal contents or even bacterial cultures from older chicks. The chicks' resistance against salmonellae increases with age[4], so it is important to protect the very young birds.

If *Salmonella* contamination occurs in the dry feed, the number of bacteria is usually very low. However, small numbers of salmonellae may be able to colonize the intestine of a very young chick but not of an older bird. A bird with salmonellae multiplying in the intestine is a dangerous carrier, effectively spreading the disease. This creates serious environmental and food-hygiene problems.

Table 2 Effect of Pretreatment and Inoculum Dose on Occurrence of *Salmonella infantis* in Three Sections of the Digestive Tract

Source of the sample	Number of salmonellae, g^{-1}	No. of chickens grouped by pretreatment and salmonellae dose			
		Pretreated		No pretreatment	
		10^3* (group A)	10^6 (B)	10^3 (C)	10^6 (D)
Crop	10^6	0	0	1	1
	10^5	0	0	1	1
	10^4	0	0	0	1
	10^3	0	0	2	2
	Only by enrichment	2	3	3	3
	Not detected	11	10	5	2
Total		13	13	12	10
Small intestine	10^6	0	0	0	1
	10^5	0	0	1	0
	10^4	0	0	0	1
	10^3	0	0	0	3
	10^2	0	0	0	1
	Only by enrichment	1	1	6	0
	Not detected	12	12	5	4
Total		13	13	12	10
Caeca	10^8	0	0	4	4
	10^7	0	0	3	3
	10^6	0	0	5	3
	Only by enrichment	0	1	0	0
	Not detected	13	12	0	0
Total		13	13	12	10

* Numbers of salmonellae given are approximate.

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Semi-dwarf Wheats induced by Monosomy and Associated Changes in Gibberellin Levels

THE genetic basis of height control in the hexaploid wheats, *Triticum aestivum* ($2n=6x=42$), is complex as shown by the study of inter-varietal chromosome substitution lines[1] and monosomic analyses[2]. Almost all twenty-one pairs of chromosomes have some effect on plant height in the tall and medium-tall varieties.

The genetic sources used in breeding dwarf and semi-dwarf varieties now popular in agriculture are "major gene" dwarfs, the most widely used being the Japanese variety, Norin 10. This dwarfism was thought to be controlled by two duplicate loci but the F_2 segregation obtained from a cross between the varieties Norin 10–Brevor 14 and Chinese Spring showed a wide range of phenotypes[3]. Monosomic analyses of the same varietal difference have implicated at least eleven chromosomes, the loss of chromosomes 2A, 2B, 2D, 3D, 4B and 4D especially resulting in a lowering of plant height.

The physiological cause of dwarfing in wheat is unknown although gibberellin (GA) metabolism is almost certainly involved. Unlike tall wheat varieties only small changes in final plant height of Norin 10–Brevor 14 occur when GA is applied[4]. Radley[5] has shown that a number of semi-dwarfs derived from Norin 10 have very high levels of free endogenous

GA compared with tall controls. Both these results suggest a block in utilization of GA in these lines.

A form of semi-dwarfism similar in morphology to that of Norin 10 is found among aneuploid lines of the semi-winter wheat variety Bersee. In a series of monosomics in which each chromosome pair in turn is represented only by a single chromosome, there are differences in height which may be ascribed to the dosage effects of individual chromosomes. The monosomics for chromosomes 2A, 2B and 2D, representing corresponding homoeologous chromosomes derived from each of the three different diploid ancestors of wheat, and carrying out similar genetic activities, are outstanding. Under glasshouse conditions they are 30% shorter than euploid in final plant height. Other features of the Norin 10 dwarfs are also apparent. Compared with the euploid phenotype, coleoptile lengths are reduced and leaves are wider and darker. Unlike the Norin 10 dwarfs, however, these monosomics respond to applied GA and to the inhibitor ethyl trimethyl ammonium chloride (CCC), which blocks the endogenous synthesis of GA (Table 1). Treatment with GA produces a larger percentage increase in the height of seedlings in the group 2 monosomics than in Bersee euploid or in the controls monosomic for other chromosomes.

Table 1 Height of Seedlings at 15 Days and Responses to GA$_3$ (10 μg ml.$^{-1}$) and CCC (100 μg ml.$^{-1}$)

	Control	+GA$_3$ Response and %	+CCC control value
Euploid	24.87 cms	+9.3 (137.4%)	−9.1
Bersee 2A	20.94*	+9.6 (145.6%*	−8.2
Bersee 2B	22.96	+9.6 (141.7%)	−8.5
Bersee 2D	21.80*	+10.1 (146.2%)*	−8.3
Bersee 5BS 7BS	23.85	+9.3 (139.1%)	−9.6
L.S.D. 5%	2.71 cms	(5.5%)	

* Significant difference from the euploid value.

The growth regulators were supplied in Hoagland's solution and the seedlings grown in continuous light at 18° C.

In two further experiments the free endogenous GA was extracted and measured in seedlings of Bersee group 2 monosomics. Table 2 shows that in both experiments the Bersee group 2 monosomics have lower levels of total free GA and that this variation is not an inevitable consequence of monosomy.

Table 2 Free Endogenous Gibberellin-like Substances Extracted from 14 Day Old Seedlings

	I	II	Final height 1971
Bersee euploid	2,310	1,570	130 cm
Bersee 2A	885*	625*	98 cm
Bersee 2B	1,210*	675*	99 cm
Bersee 2D	755*	—	98 cm
A and B genome monosomics excluding group 2	—	1,273	

* Significant difference from the euploid value.

Plant material was homogenized in buffer at *p*H 8.6 and extracted with ethyl acetate at *p*H 3.0. This acid fraction was concentrated and chromatographed on paper in isopropanol, NH$_3$, water (10 : 1 : 1) and the RF segments containing GA$_1$ + GA$_3$-like activity were tested in the barley endosperm bioassay[6]. Two replicate extractions were assayed in experiment I and three replicates of all A and B genome monosomics in experiment II. Total GA is expressed as GA$_3$ pg equivalents gm^{-1} fr. wt.

These results could be explained if the group 2 chromosomes control some part of the metabolism of GA, probably biosynthesis and, in the monosomic condition, limit the availability of GA. This would produce similar effects in plant height to the block in utilization postulated for the Norin 10 based semi-dwarfs.

The differences in GA levels between the two kinds of semi-dwarf and also their different responses to applied GA and CCC could indicate that the underlying genetic causes of the Norin 10 dwarfing are not associated with allelic variation among loci carried on the group 2 chromosomes. Although monosomic analyses involving semi-dwarf wheats as one of the parents[3] have implicated these chromosomes in the control of height differences, it must be remembered that such analyses confound both allelic and chromosome dosage differences. Under such circumstances the group 2 chromosomes are likely to feature markedly although allelic variation may not be present.

Another observation possibly related to the influence of group 2 chromosomes on GA levels concerns investigations into plant survival in response to freezing among monosomic lines of the variety Cappelle-Desprez[7]. It has been shown[8,9] that application of GA by soaking the seeds or by spraying the seedlings of tall varieties stimulates growth and reduces the level of cold resistance. Similarly, treatment with CCC, presumably by lowering endogenous levels of GA, increases the level of cold resistance. Among the monosomics of Cappelle-Desprez tested for their cold resistance the only representative of group 2 tested, chromosome 2A, showed increased resistance; it is probable that this increased resistance could be due to the low levels of GA brought about by the reduction in chromosome dosage. Further support for this effect of chromosome dosage derives from the analysis of cold resistance among inter-varietal chromosome substitution lines of Cappelle-Desprez in a Chinese Spring background[10] in which the effect of chromosome 2A in the disomic state was not apparent.

It seems likely that in wheat, semi-dwarfism may be accomplished either by reducing synthesis of GA or by reducing the availability of the GA present as in the Norin 10 based dwarfs. The different levels of GA present as free endogenous hormone which are a consequence of these two types of height control may affect developmental processes other than height. It is possible from an understanding of these differences that an explanation of the recent agricultural successes of the semi-dwarf wheats will be found.

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Tool-use in Free-living Baboons in the Gombe National Park, Tanzania

AN animal may be said to use a tool when an object is used as a functional extension of the hand (or claw, mouth, beak) in the attainment of an immediate goal[1]. References have been made to tool-using in wild baboons. Marais[2] describes the manner in which the individuals of one troop of baboons

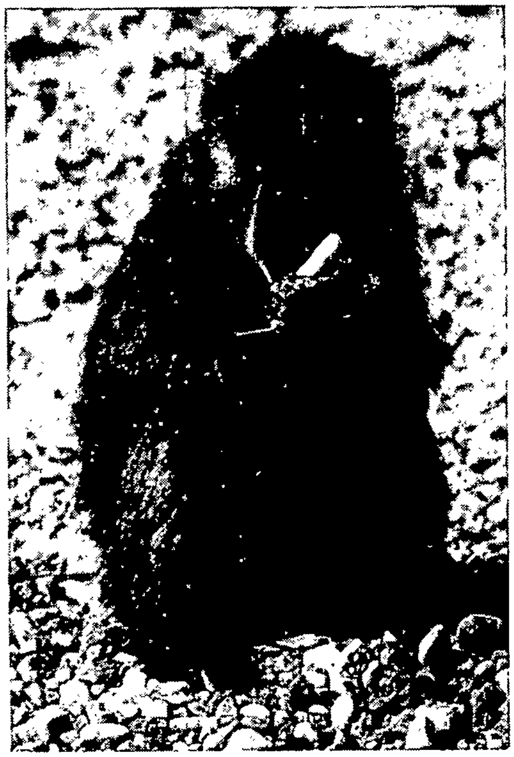

Fig. 1 Clover (3 yr old female baboon) using a stone to wipe her mouth after feeding. (Photo: C. Packer)

(*Papio ursinus*) broke open the hard-shelled fruits of "sausage trees" (*Kigelia pinnata*) with rocks in order to feed on the seeds. Kortlandt and Kooij[3] mention one baboon using a stone to squash a scorpion to eat it, and another using a stick to prod about in a termite nest. In these two instances no details of the behaviours nor of the conditions under which they were observed are given so that they should probably not be accepted as wholly reliable.

There are few reports of tool-use in captive baboons. Bolwig[4] describes one individual (*P. ursinus*) who used a stick to rake in food out of reach; he recorded purposefully aimed throwing in the same baboon. Kortland and Kooij[3] collected twelve reports of apparently aimed throwing in zoo baboons.

Recently a new tool-using performance has been twice observed in the olive baboons (*P. anubis*) at the Gombe National Park, Tanzania, involving the use of an object for wiping the mouth. To feed on the seeds of *Diplorhynchus condylocarpon* the baboons must break open the tough-shelled pod in which the seeds are surrounded by a white glutinous juice drying to form a rubbery cement. When this food is in season, the baboons are frequently seen with the hair around their lips matted by the juice to which pieces of pod or leaf often adhere. Often they will pause to rub their dirty mouths against a tree trunk or large rock.

One three-year-old female, however, picked up a fairly large stone with which she repeatedly and forcefully rubbed at her muzzle in an attempt to remove the dried juice (Fig. 1).

The second incident, observed about one month later, involved an adult male of a different (neighbouring) troop. He cut his lower lip during a fight, causing blood and saliva to run down his chin. When, presumably, the blood had begun to coagulate, the baboon looked around, reached out for an old piece of maize kernel (the troop was foraging around human habitation) and with this gently wiped away most of the blood from his lower lip. Whilst we cannot draw conclusions from one episode it is interesting that, although there were several stones nearby, this baboon selected a softer, more porous and generally more suitable material.

The only other non-human primate which has been observed using objects as "napkins" in this way is the chimpanzee[1,3]. At the Gombe Stream the chimpanzees typically use leaves to wipe dirt or blood from their bodies. Like the baboons, they also feed on the seeds of *Diplorhynchus condylocarpon* but, whilst they have been observed to rub their mouths against tree trunks and to indulge in a variety of facial contortions in an endeavour to remove the juice around their mouths with their lips and teeth, they have not, to date, been observed to use any objects as wiping tools in this context.

Admittedly we have only observed two individual baboons using objects in this way but because each belongs to a different troop, and because after the first event relatively little time elapsed before the behaviour was noticed again, it may occur fairly commonly. It is an action which would be extremely easy to overlook, and we draw attention to it here in order that other scientists working in the field may be aware of this behaviour. The research was financed by the Grant Foundation and Stanford University.

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Effect of Seawater Soluble Fraction of Kerosene on Chemotaxis in a Marine Snail, *Nassarius obsoletus*

In aquatic environments, behaviour such as food finding, reproductive activities and orientation may depend on an organism's detection of specific chemical cues. One of the dangers of the increasing load of pollutants in the sea is that natural chemically mediated behaviour important in the lives of marine animals may be disrupted by minute amounts of these contaminants. This possibility has been suggested for chronic pollution by oil, whose sublethal effects are little known[1]. To examine quantitatively behavioural disruption by oils, we have investigated the effect of the seawater-soluble fraction of kerosene on the attraction of the marine prosobranch snail, *Nassarius obsoletus*, to food extracts. This snail has already been found to be quite suitable for studies of chemoreception[2,3]. Kerosene seawater extract was selected because its components have been identified and quantified and are also present in seawater extracts of some crude oils[4].

Nassarius obsoletus were collected in the autumn of 1970 and spring of 1971 at several locations on Cape Cod, Massachusetts. During the autumn, they were held in flowing seawater at 14–15° C and fed occasionally on crushed *Mytilus edulis* for 6 weeks before experiment 1. During the spring, *N. obsoletus* were kept in heated seawater at 14–15° C without food for 10 days before experiment 2.

The experiments were performed in an acrylic plastic Y-chamber with equal angles between the arms, which were 42 cm long and 10 cm high and wide. Two upstream arms received seawater flowing at 1.5 l. min^{-1} (14–15° C); one was selected randomly as the stimulus arm for each trial. In this arm, seawater was pre-mixed with stimulus solutions in the first of two mixing chambers. A rhodamine B flow profile indicated that complete mixing occurred in the stimulus arm. In the downstream arm, mixing was incomplete although laminar flow was rarely observed.

Seawater extract of kerosene was prepared as described by Boylan and Tripp[4] by slowly stirring a layer of 25 ml. kerosene (Gulf Oil Co. grade) over 1.5 l. seawater for 12 h, and separating the aqueous and oil layers. The seawater-soluble kerosene extract, consisting mostly of benzenes and naphthalenes, was calculated to contain about 610 µg of oil/l. seawater[4]. The kerosene extract used in experiment 1 was prepared in this manner. For experiment 2, kerosene seawater solubles were extracted with pentane four times, the pentane removed by rotary evaporation, and the residue mixed with 300 ml. seawater, in an attempt to concentrate the extract.

In experiment 1, there were four treatments: attractant, seawater control, kerosene extract and attractant plus kerosene extract. The attractant, oyster (*Crassostrea virginica*) extract, was prepared by Soxhlet extraction of the soft parts and extra pallial fluids with methanol for 6 h, filtering (0.45 µm 'Millipore'), and concentrating *in vacuo*. The concentrated extract was desalted on a 'Dowex 50 W-X12/1-X8' column equilibrated with ammonium bicarbonate. The nonretained effluent was freed from ammonium bicarbonate by repeated evaporation *in vacuo* and stored at −20° C. The quantity of extract obtained was 1 ml./1.6 oysters. Stimulus solutions for attractant and attractant plus kerosene treatments were prepared by diluting 0.0125 ml. of oyster extract in 110 ml. seawater or kerosene seawater extract. Equal volumes of seawater or kerosene extract alone were used in control and kerosene treatments. These solutions flowed at a constant rate of 2.5 ml. min^{-1} from a flask inverted into a syringe fitted with a No. 20 needle. The concentration in the stimulus arm of kerosene extract was calculated at 1 part 10^{-9} (p.p.b.), and of oyster extract (wet weight basis) about 0.33 parts 10^{-6} (p.p.m.).

Table 1 Experiment 1

	Attractant (oyster extract)	Attractant+ kerosene extract (1 p.p.b.)	Kerosene extract (1 p.p.b.)	Control (seawater)
Stimulus arm $\bar{x}\pm$s.e.	4.4±1.0	1.7±0.3	1.0±0.5	0.8±0.8
Nonstimulus arm $\bar{x}\pm$s.e.	0.6±0.4	1.3±0.3	1.7±0.7	0.3±0.3
Number of trials (ten snails per trial)	5	3	3	4

Mean ±s.e. of number of *N. obsoletus* in stimulus and nonstimulus arms in each treatment at 15 min. Means joined by underlining are not significantly different at or below the 0.05 protection level using Kramer's modification of Duncan's multiple range test[5].

Experiment 2 included the same four treatments. An attractant was prepared from homogenized adductor muscle of the scallop *Aequipecten irridians* (2 g in 100 ml. seawater, filtered through a 'Pyrex' glass filter and refrigerated). All tests were run within 1.75 h of preparation of the attractant. For the attractant and attractant plus kerosene treatments, 5 ml. of scallop homogenate was diluted with 45 ml. of seawater or kerosene extract respectively; 5 ml. of seawater was added in the control and kerosene experiments. These solutions were introduced at 2.3 ml. min^{-1}. Concentrations of kerosene extract and scallop homogenate (wet weight basis) were calculated at 4 p.p.b. and 3 p.p.m. respectively.

The attractant and control treatments were run before the experiments in which kerosene extract was used, due to possible adsorption of small amounts of kerosene components on the walls of the Y-chamber and glass. In experiment 2, the chamber was scrubbed with hot water following each trial to remove slime trails and adsorbed kerosene components.

The experiments differed slightly in procedure. In the first experiment, ten specimens of *N. obsoletus* were lowered gently in a Petri dish into the base of the lower arm 2 min after introduction of the stimulus solution. The position of the snails was recorded at 5 min intervals for 30 min. In the second experiment, each trial lasted 15 min; the snails were introduced halfway up the lower arm. Those reaching a line halfway up either upper arm were removed with forceps, scored as responding positively, and the time noted. In all experiments, snails were used for one trial only.

Table 1 shows the results of experiment 1, 15 min after the introduction of snails, when the mean number attracted to oyster extract alone reached an asymptote. In the presence of 1 p.p.b. kerosene extract, attraction to oyster extract was reduced to a level not significantly different from the control or kerosene treatments. The number of snails observed in the nonstimulus arm did not differ significantly between treatments. In all treatments, half or more of the snails remained in the lower arm; most crawled about actively. No difference in behaviour was observed between snails exposed to kerosene extract alone or to seawater. Although *N. obsoletus* can follow mucus trails of conspecifics[2], at least 50% of the snails in the attractant treatments did not follow the other snails into the upper arms; in the other treatments, snails entered either arm about equally (Table 1).

Table 2 Experiment 2

	Attractant (scallop homogenate)	Attractant+ kerosene extract (4 p.p.b.)	Kerosene extract (4 p.p.b.)	Control (seawater)
Stimulus arm $\bar{x}\pm$s.e.	7.0±0	4.8±0.9	0±0	0.6±0.6
Nonstimulus arm $\bar{x}\pm$s.e.	0.2±0.2	0±0	0±0	0.3±0.3
Number of trials (ten snails per trial)	5	4	2	3

Mean±standard error of number of *N. obsoletus* responding positively in stimulus and nonstimulus arms in each treatment. Comparison of the attractant and attractant plus kerosene treatment means using the Mann-Whitney U test[8] showed that they were significantly different below the 0.05 level.

As Table 2 shows, in experiment 2 there was a significant reduction in attraction to scallop homogenate in the presence of kerosene extract. Results of a previous experiment of the same format had shown that kerosene extract at 0.8 p.p.b. was not similarly effective.

Seawater extracts of several crude oils have low boiling components similar to those in kerosene seawater extract[4]. Although little has been published on concentrations of oil in seawater, values for dissolved Bunker C oil have been determined 3 months after a spill in Chedabucto Bay, Nova Scotia. Concentrations for stations up to 20 miles from the spill site ranged from less than 10 to 90 p.p.b.[7]. Naphthalenes, the major components present in kerosene seawater extract, have been reported in concentrations around 1 p.p.b. in the polluted Charles River Basin, Boston. Naphthalenes are known to be acutely toxic[4,8] and may have altered the behaviour of *N. obsoletus* in the present experiments, perhaps through interference with chemoreception.

The two experiments reported here demonstrate that minute quantities of the seawater-soluble fraction of kerosene interfere with the chemically mediated attraction to food extracts in *Nassarius obsoletus*. Oil components may disrupt chemically mediated behaviour in organisms of widely separated taxa: dilute concentrations of diethyl ether extracts of crude oils inhibit the feeding response and sex pheromone response in the lined shore crab, *Pachygrapsus crassipes*[9]. Our results suggest that there is need for further research on the effects of oil pollutants on chemically mediated behaviour of marine animals.

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Lead Accumulation within Nuclei of Moss Leaf Cells

THE accumulation of lead within vegetation growing near busy roads has for some years received considerable attention[1–4]. Less effort, however, has so far been made to find out where in the plants accumulation takes place, an important question when the subsequent effects of heavy metal pollution are to be considered.

We based our study upon the electron scattering properties of heavy metals such as lead. It was postulated that as lead is used as a stain in routine electron microscopy the presence within cells of lead derived from pollution might be revealed directly from transmission electron micrographs, provided that the local concentration of the metal in the cell was high enough and that no heavy metal stains were used during the initial preparation. As bryophytes are known to accumulate heavy metals in concentrations which are toxic for other groups of plants[5,6], mosses were chosen as the experimental material.

In a pilot study, specimens of *Rhytidiadelphus squarrosus* (Hedw.) Warnst. were cultivated in a greenhouse and watered once a day for three weeks with a series of lead acetate solutions (providing concentrations of 100–1,000–10,000 p.p.m. of lead). A control series was watered with tap water. Leaf samples were taken at one-day intervals. They were pre-fixed in 2.5% glutaraldehyde for 4 h, post-fixed in osmium tetraoxide for 3 h, rinsed in cacodylate buffer after each fixation, dehydrated in acetone, embedded in 'Epon' and sectioned on an 'LKB-ultratome'. A 'JEM 100B' transmission electron microscope was used.

A comparison of electron micrographs from unstained polluted material with micrographs from leaf cells from the control samples revealed electron-dense inclusions in the cells from the lead-treated samples, while no such inclusions were found within cells from the control series. These electron-dense inclusions could also be recognized after post-staining the sections with uranyl acetate or lead citrate so as to enhance the contrast.

A similar investigation was made on lead-polluted material of *R. squarrosus* collected from a park in Trondheim about 250 m away from a relatively busy city road.

Within the nuclei of the leaf cells we repeatedly found electron-dense particles. Fig. 1 shows numerous inclusions and damage to the nuclear membrane. Fig. 2 shows a leaf cell from this same moss cultivated under unpolluted conditions in the laboratory.

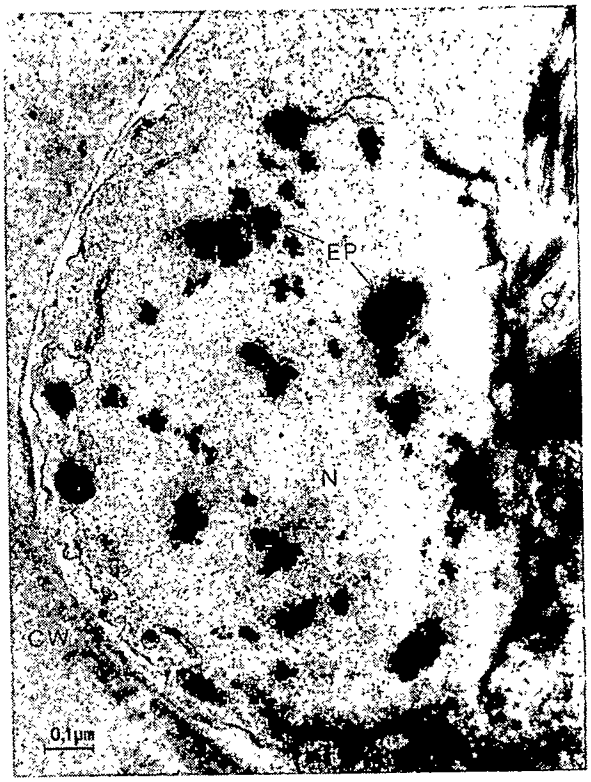

Fig. 1 Electron micrograph of leaf cell of *Rhytidiadelphus squarrosus*, collected from a park near a busy main road. The nucleus contains many electron-dense particles shown by means of 'EMMA' to contain lead. The nuclear membrane is damaged. The section has not been post-stained. CW, Cell wall; C, chloroplast; EP, electron-dense particles shown by X-ray microanalysis to contain lead; N, nucleus.

The electron-dense inclusions found within the nuclei of moss cells from the park area were believed to represent lead complexes, an assumption based on the following arguments: (1) Chemical analysis of the moss leaves showed a lead content of about 50 p.p.m. (dry weight). (2) Similar inclusions within cell nuclei are not known to be a normal part of plant cell ultrastructure. (3) When mosses from the same locality as those containing the electron-dense inclusions were cultivated in Petri dishes under normal "unpolluted" conditions in the laboratory, they developed shoots in which no similar electron-dense inclusions were found within the cell nuclei. (4) In an autoradiographical study, Dallenbach[7] showed that isotopic lead (^{210}Pb) was incorporated into the cell nucleus. In a cell fractionation study, using tracer technique[8], the lead isotope was found to be incorporated in the organelles of the nuclear and mitochondrial fractions. (5) In a series of fine structural investigations of experimental

Table 1 X-Ray Analysis of Electron-dense Inclusions

	Peak (Pb L_α line) (P)	Background (b)	P–b
	263	76	
	312	57	
	295	71	
	290	60	
	299	64	
Mean	292	66	226

The height of the characteristic L_α line for lead is given as the difference between the peak value (P) and the background (b). This difference, P–b, represents a direct measure for the quantity of lead present in the analysed material.

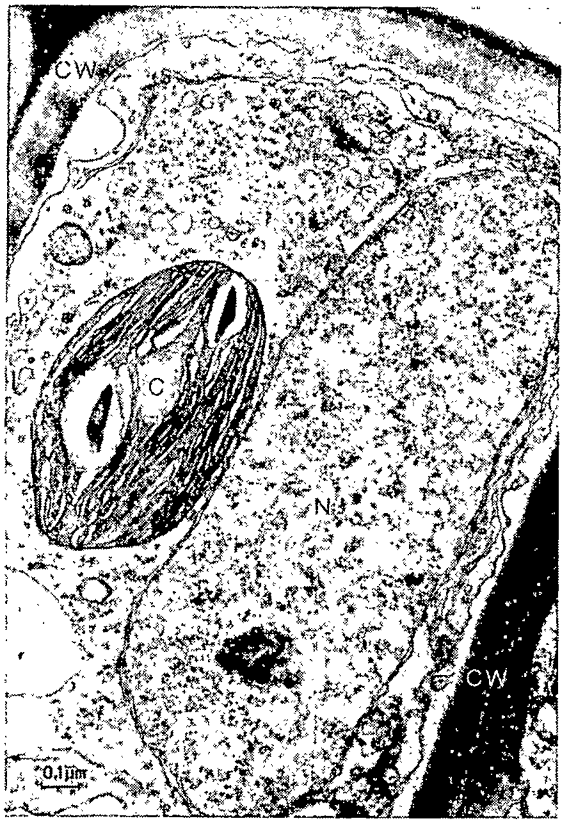

Fig. 2 A leaf cell from the same moss species grown in unpolluted conditions. Lettering as in Fig. 1.

lead poisoning with rats[9–12], similar inclusions were found within cell nuclei of the tubular cells of the kidney. Goyer isolated these inclusions and found that they consisted of a lead-protein complex.

To validate our claim, an X-ray analysis of the electron-dense inclusions, using an 'EMMA' (electron microscope microanalyser), was carried out by the AEI consultant laboratory. The analysis confirmed that the electron-dense particles found within the nuclei did contain lead (Table 1).

Other areas in the cytoplasm which showed electron-dense precipitates were also examined, but with a single exception no lead could be demonstrated. In this one area the mean characteristic peak was 46 compared to the background of 22, giving a $P–b$ value of 24. The aim of our study was to investigate the possibility of locating heavy metal residues—in this case lead—derived from atmospheric pollution within plant cells and organelles, using transmission electron microscopy. Our findings that lead is incorporated into the nuclei of lead-polluted moss cells agree with previous findings of lead inclusions within the nuclei of tubular cells from the kidneys of lead poisoned men and animals[9–13]. The binding of lead within the nuclear membrane, as a non-diffusible complex, has been suggested as the mechanism whereby the cytoplasmic concentration of diffusible lead substances within the cell can be kept below a level that would otherwise be toxic to the mitochondrial and other lead-sensitive functions of the cytoplasm, or as stated by Goyer: "This mechanism may be relevant to man's adaptation to his chronic body burden of lead". We suggest that the same mechanism may apply to plants.

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The Single Atom Spectrometer and its Application in Chemistry and Biology

MUCH work has been done on damage in solids caused by particulate and non-particulate radiation; however, the subsequent effect on the environment has been neglected. I have demonstrated[1–3] that material can be transferred to an emitter whose electrons bombard a solid, and that single atoms and complexes liberated can be detected by the fluctuations they cause in the field emission when they impinge on the emitter. The present work was directed to detecting, recording and identifying these entities; in short, to the design of a single atom spectrometer.

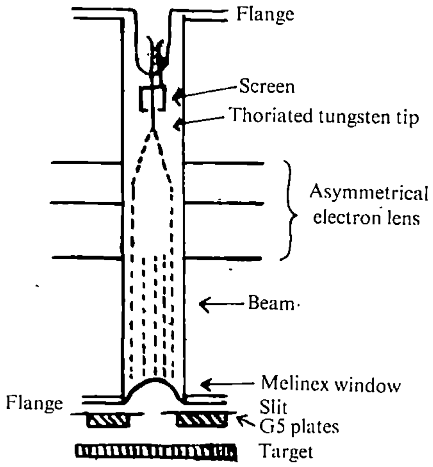

Fig. 1 Experimental tube.

In the experimental work, the radiation source was an etched thoriated tungsten point of some 3000 Å radius, from which field electrons are emitted into a good vacuum by an external asymmetrical three element electron lens used in the "Einzel" condition. The nearly parallel beam (current density ~1 μA cm^{-2} at 55 kV) emerges through a 'Melinex' window and bombards the target in air. This is placed below a masked-off slit collimating system, 15×1 mm, with Ilford G5 emulsion plates on its underside, 0.5 mm from the slit, as a detector. The scheme of experimental arrangement is shown in Fig. 1 where the spacing between the emulsion and target was kept at 0.1 mm and a field of 3–6 kV cm^{-1} was placed between target and slit system.

When the plates are processed, they show the blackening

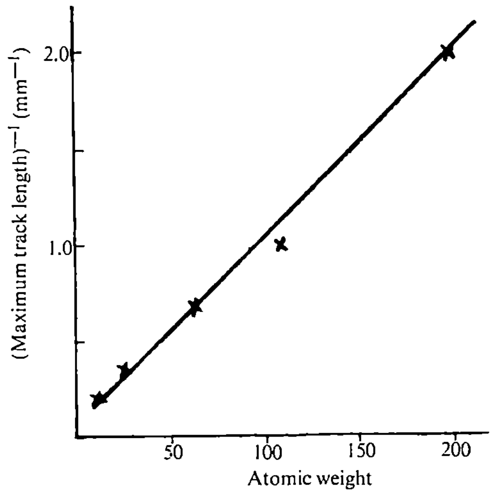

Fig. 2 Relation between (maximum track length)$^{-1}$ and atomic weight.

expected near the edges closest to the slit from back-scattering effects, together with what appear to be a series of tracks of variable length, some curved, some straight, all of which seem to be characteristic of the target material and the impurities it contains. On the simple basis of momentum exchange, it would be expected that atoms or complexes liberated by bombardment would have a whole spread of energies almost up to the maximum of the incident beam. These would not travel any measurable distance in the emulsion, but, if channelled through the air, in directions nearly parallel to the surface of the emulsion, would be expected to have path lengths of a few tenths of a millimetre; indeed, the track lengths in the emulsion are of these magnitudes.

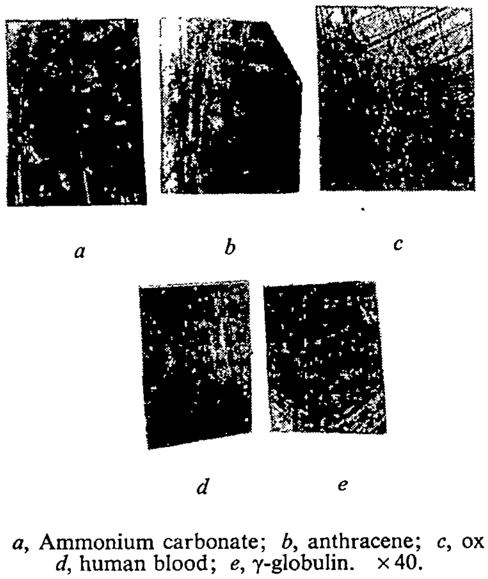

Fig. 3 *a*, Ammonium carbonate; *b*, anthracene; *c*, ox liver; *d*, human blood; *e*, γ-globulin. ×40.

As, for a fixed energy, the energy loss of similarly charged particles varies with the mass, the range in air should vary inversely as the mass. It was found that, using targets of carbon, aluminium, copper, silver and platinum, the corresponding maximum track lengths in the emulsion also varied approximately inversely as the mass as shown by the rough calibration of Fig. 2.

A tentative proposal explaining the presence of tracks and accounting for the observed lengths is as follows. The back-scattered electrons from the target produce 'F' centres in the emulsion, and the available electrons are guided through the emulsion by the field of those charged liberated atoms or complexes which happen to move in a direction very close to its surface (the field of a singly charged atom at some 10 Å from the surface is of order 10^9 V m^{-1}). The tracks in the emulsion would then delineate the paths of the charged liberated particles in air, and their lengths would give a measure of the masses of the atoms or complexes which produced them.

The interest for the chemist lies in the possibility of detecting impurities in his materials on an atomic scale, disintegration products of radiation damage or preferred orientations of released particles. For the biologist, the technique offers a method for following up changes in living cells under different biochemical conditions, radiation damage in tissue, the effects of missing atoms or groups on reactions of biological importance.

The compounds so far studied include graphite, ammonium carbonate, glucose, phenol, apiezon grease, paraffin wax, iodoform, iodine, urea, thiourea, salicylic acid, ox liver, egg white and yolk, β-naphthalamine, human blood, γ-globulin, and anthracene. As examples, tracks from the last three compounds together with those from ammonium carbonate and ox liver are shown in Fig. 3. The preferred direction of liberated atoms from anthracene is parallel to the slit edge and the majority of tracks show liberated carbon atoms; the longest are identified with liberated protons. The possibility of recording impurity atoms present in metal specimens is revealed by the study of tracks obtained with laboratory specimens of metals.

I thank ICI (Welwyn Garden City) for supplying the 'Melinex' plastic for the window. Full details will be published elsewhere.

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Dinoflagellates near the Cretaceous Jurassic Boundary

MANY well-preserved dinoflagellate fossils occur in Jurassic and Cretaceous marine sedimentary sections of various lithologic characteristics in the western North Atlantic and the western side of the Sacramento Valley of California[1,2]. We have discovered five species which are common to the two sections—as first noticed by W. R. Evitt—each occurring in the Cretaceous above the Cretaceous/Jurassic boundary, and not in the subjacent Jurassic (Fig. 1). These species are *Biorbifera johnewingi* Habib, *Dingodinium cerviculum* Cookson and Eisenack, *Scriniodinium attadalense* Cookson and Eisenack, and two as yet unnamed species, *Polysphaeridium* sp. and *Pyxidiella* sp. Two of the five species, *B. johnewingi* and *Polysphaeridium* sp., were found to range through most of the Berriasian (lowermost stage of the Cretaceous System) at its type locality in southern France. *B. johnewingi* satisfies the requirements of a stratigraphically useful guide fossil especially well; it is morphologically distinctive, geographically widespread, relatively abundant in the three areas of investigation, and of limited stratigraphic range (Berriasian-middle Valanginian). Furthermore, it first appears very near the Cretaceous/Jurassic boundary at the three localities. A sixth species, *Occisucysta?* sp., appears to be discordant, being confined to the uppermost Jurassic in California and the lowermost Cretaceous in the North Atlantic.

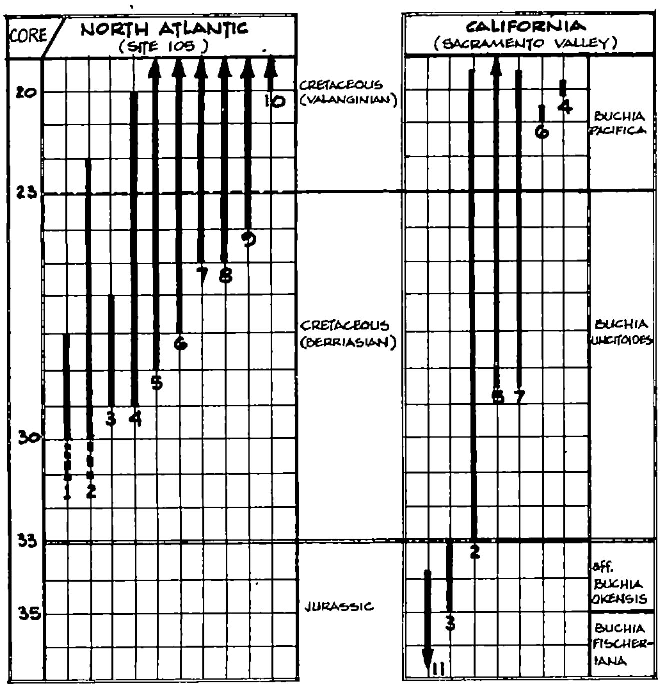

Fig. 1 Comparative dinoflagellate stratigraphy, North Atlantic and California. 1, *Cyclonephelium* sp.; 2, *Biorbifera johnewingi*; 3, *Occisucysta*? sp.; 4, *Pyxidiella* sp.; 5, *Polysphaeridium* sp.; 6, *Scriniodinium attadelense*; 7, *Dingodinium cerviculum*; 8, *Scriniodinium campanula*; 9, *Cyclonephelium distinctum*; 10, *Oligosphaeridium complex*; 11, *Belodinium dysculum*.

The fossils discussed above were observed at the four sites which yielded Lower Cretaceous sediments in the North Atlantic[3]. At site 105, which was drilled at abyssal depths approximately 380 miles east of Cape Hatteras, North Carolina (34° 53.72′ N; 69° 10.40′ W), coring was nearly continuous through partly recrystallized greyish-white to white nannoplankton chalk, and passed through the Cretaceous/Jurassic boundary. Based on calpionellids, the upper part of core 33 (Fig. 1) is considered to be very near the boundary, with preference to the lower Berriasian[4]. Dinoflagellate cysts are numerous and diverse through the Cretaceous down to core 30, below which they are rare. The interval between this core and the calpionellid boundary in core 33 is approximately 27 m. Dinoflagellates are abundant again lower down in samples of undisputed Jurassic age (core 35). None of the five species listed above was found in these samples, even though the assemblages are equally fossiliferous.

Table 1 Geographic Distribution of Stratigraphically Important Lower Cretaceous Dinoflagellates

Species	California	N. Atlantic	S. France
Biorbifera johnewingi	×	×	×
Polysphaeridium sp.	×	×	×
Dingodinium cerviculum	×	×	
Pyxidiella sp.	×	×	
Scriniodinium attadelense	×	×	
Scriniodinium campanula		×	×
Cyclonephelium distinctum		×	×
Cyclonephelium? sp.		×	×
Oligosphaeridium complex		×	×
Diacanthum hollisteri		×	×

Four other species that first appeared in the Cretaceous at site 105 are also present in the Berriasian type section, though not in California (Table 1). These are the following: *Cyclonephelium distinctum* Deflandre and Cookson, which ranges through most of the type section, *Cyclonephelium?* sp., which is apparently restricted to the lower and middle parts of the type section; and *Scriniodinium campanula* Gocht, which was found in the uppermost sample of the type Berriasian and in the Valanginian above; and *Diacanthum hollisteri* Habib. In addition, *Oligosphaeridium complex* (White) is present in the Valanginian at the Berriasian stratotype locality, as it is also at site 105.

Dinoflagellates are common and well preserved in the Upper Jurassic and Lower Cretaceous rocks of the Great Valley sequence of California. This sequence is located on the west side of the Sacramento Valley, and consists of up to 40,000 foot of interbedded grey sandstones and dark grey mudstones, with numerous layers of limestone concretions[5]. The Upper Jurassic (Tithonian) through lower Lower Cretaceous (Berriasian-Valanginian) portion has been subdivided into six zones, based upon the succession of species of the pelecypod genus *Buchia*[6]. *Buchia* is generally a northern form, being found in California, the Pacific northwest states, Canada, the Russian platform and northern Europe, but not, however, in the stratotype sections of the Jurassic and Cretaceous stages in southern Europe south of northern France. Therefore, any age determinations based solely on *Buchia* may be suspect. Fortunately, ammonites are present in the Great Valley sequence, and afford fairly precise age determinations of the *Buchia* zones[7].

In California, *B. johnewingi* appears virtually at the base of the Cretaceous System. *Polysphaeridium* sp. and *D. cerviculum* first appear at the top of the lower third of the Berriasian, somewhat earlier than their first appearance in the North Atlantic. *S. attadelense* and *Pyxidiella* sp. have more restricted ranges, and appear higher in the section; however, they occur within their corresponding North Atlantic ranges. An additional species, *Belodinium dysculum* Cookson and Eisenack, is confined to the Tithonian, just below the boundary. This species was described as "probably Tithonian" from the Upper Jurassic of Australia[8].

We conclude that the five Cretaceous species occurring mutually in California and the North Atlantic, as well as the additional species discussed in this report, are potentially valuable guide fossils. *B. johnewingi* is the most important, because it appears directly above the Cretaceous/Jurassic boundary in the two sections and also in the lower part of the Berriasian stratotype section. The similar succession of species in widely separated areas, and their close relationship to the Cretaceous/Jurassic boundary, emphasizes the contribution dinoflagellates make to Mesozoic stratigraphy on the continents and in the ocean basins.

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BOOK REVIEWS

English Science Policy

The Organisation of Science in England. By D. S. L. Cardwell. Pp. xii+268. (Heinemann Educational Books: London, October 1972.) £2.80. Revised edition.

FIFTEEN years after Dr Cardwell's *The Organisation of Science in England* first appeared we now have a revised edition (a paper-back version of which is issued as an Open University set book). Although it incorporates a good deal of recent scholarship on the social history of 19th-century British science, the argument of the book remains fundamentally unchanged.

The process by which English science was transformed from the "amateur" pastime of 1800 into the professional enterprise of the present day is the story of success over remarkable adversity. Reliance on individualism, voluntarism and self-help was reinforced by a deep-rooted suspicion of State intervention which made Victorian men of science initially reluctant to demand Government support of research. Government, on the other hand, did not, until quite late in the 19th century, recognize scientific research as something essential to national welfare. As late as 1869 the Chancellor of the Exchequer refused a request for a mere £300 from a meteorological society with the icy pronouncement that it was "our duty not to spend public money to do that which people can do for themselves".

Yet throughout the century statesmen of science like Babbage, Playfair, Tyndall and Huxley were vigorously arguing the dependence of national progress on the endowment of research, both pure and applied. What was good for the professionalization of science was good for Britain and State subvention was necessary. In 1878 Colonel Strange claimed that "the tendency of progressive civilization must be to supersede individual effort", and four years later Sir B. C. Brodie announced, with typical hyperbole, that a class of professional researchers "does not exist among us and its absence is the greatest defect in our social system". Continental models came to the aid of a characteristically British capacity for self-criticism. German liberality in the support of science and applied science was the most frequently cited example of what Britain ought to be doing for her men of science. But it was not until the Great War that the consequences of British parsimony became fully evident.

The most intriguing theme of Dr Cardwell's book is the congruence between the professionalization of science and the reform of English education. While scientific training of the highest quality was always available to the upper classes, it was not until elementary, secondary and technical education was vastly expanded that England could produce the requisite "rank and file" of the scientific enterprise as well as the "officers". And, until the lower levels of education received adequate support, English science could not offer trained men of science the teaching positions which professional science requires.

Cardwell's work is still the most thorough and competent treatment of the subject available. Good as it is, it may be criticized on two main heads. First, it must be recognized that the relevant policy for professionalizing 19th-century science is Britain and not England. The bleak portrait Cardwell paints of the early institutional standing of science might have been quite different had the Scottish situation occupied more than a peripheral place in his account. Second, one feels that Cardwell has been unnecessarily harsh about early century "amateurism" and "dilettantism". The spread of scientific culture across the British landscape, notably in the form of the "literary and philosophical societies", very probably had quite a lot to do with emerging public approval of science as something to be encouraged and supported. "Amateurism", and a favourable public image of science, was probably a necessary pre-condition for later "professionalism". Cardwell focuses on the politics of professionalizing science but gives the reader very little feeling for the social and cultural background against which the process unfolded.

STEVEN SHAPIN

Pattern Recognition

Fundamentals of Pattern Recognition. By Edward A. Patrick. Pp. xxiv+504. (Prentice-Hall: Englewood Cliffs, New Jersey; Prentice-Hall International: London, 1972.) £9.

THIS book is concerned with purely statistical approaches to the design of systems which, given specimen vectors belonging to distinguishable clusters or classes, will automatically classify any further given vector of the same dimensionality. The classification of the specimen vectors may or may not be known *a priori*, and in cases where it is unknown we are confronted with the essential problem of numerical taxonomy.

A 115-page chapter is devoted to techniques for estimating statistical parameters. The other main topics of the book are decision rules, non-parametric techniques, clustering techniques, and dimensionality reduction. The mathematical level is fairly advanced, and the treatment is for the most part thorough, rich in theoretical insight, and unusually coherent. Anyone who has fairly advanced mathematical accomplishments and is specifically interested in the theory of the statistical approach to pattern recognition will find this book valuable: in some respects more so than *An Introduction to Statistical Pattern Recognition* by K. Fukunaga (Academic Press, New York and London, 1972).

When patterns are subject to severe distortion, it is seldom useful to apply statistical techniques directly to digitized versions of the data. It is usually better to apply statistical techniques to vectors whose components are results of distortion-invariant tests on the raw data. To select adequate tests which are more or less invariant to distortion, it has been necessary in practice to use *a priori* intuitive knowledge of distortion. This knowledge is of vital practical importance and has to be imported from outside a purely statistical framework such as Dr Patrick's. Dr Patrick is aware of this: he constantly advocates making maximal use of *a priori* structural knowledge, and in chapter seven he introduces a method for testing hypothesized structural relationships. But this does not tell us positively and specifically how to deal with highly correlation distortion. Because distortion raises by far the biggest fundamental and practical difficulty in many applications, and because Dr Patrick scarcely tackles this difficulty, a safer title for his book would have been "Fundamentals of Statistical Pattern Recognition'.

J. R. ULLMANN

Cerebral Iconography

An Illustrated History of Brain Function. By Edwin Clarke and Kenneth Dewhurst. Pp. 154. (Sandford Publications: Oxford, 1972.) £5.50.

MEDICAL-historical iconography is not only a pictorial history of observations, discoveries and cures but also, and perhaps more informatively so, of ideas. Nothing can be more explicit about this than the remarkably well devised and annotated atlas of historical illustrations of brain function under notice.

Looking into the history of ideas, the most interesting point is that it took only a little more than fifteen years to perform the long jump from rigidly unrealistic and schematic mediaeval delineation of sensory perception, imagination, rational thinking and memory in circles on the surface of the head to the realistic-observational and basically modern representation of the brain (Magnus Hundt, *Anthropologium*, 1501, to Laurent Fries, *Spiegel der Artzny*, 1518). Moreover this was achieved twenty-five years before Vesalius's *Fabrica* and a little more than twenty years before such pre-Vesalians as Dryander. The mediaeval idea was that of "cellular location", that is, the reservation of the brain ventricles for the functions: sensorium and sensory-conditioned imagination in the largest (lateral—"anterior") spaces, rational thinking in the narrowest sieve-like (middle) and memory in the most remote, posterior cell. This idea was brought about by a strange mixture of ancient Alexandrian and Galenic *pneuma* (spirit)—theories with materialistic connotations linking certain functional differences with different regions and textures. It appealed to the Fathers of the Church (Nemesius) and ever since ruled for more than a thousand years.

As the authors most aptly show, it had not died with the opposition by the great anatomists, but survived in texts and illustrations not only with the mystical crypto-mechanist Fludd, but into the times of phrenology in the early nineteenth century when the mediaeval model was suitably revised and reproduced in the translation of Blumenbach's *Physiological Institutions* by John Elliotson (1789–1868). Talking about progress we are well reminded at the end of the mediaeval chapter in the caption of a normal ventriculogram of today that the "cells" are now known to be receptacles of the cerebrospinal fluid, but that "the exact nature of its production and function is still not fully understood". Nor would it be otiose to probe into the ideological motives that account for the popularity and long persistence of ventricular localization—a subject naturally outside the scope of the present work. A certain mediaeval—schematic—touch remains in at least one of the illustrations of the persistently overrated physiological speculator Descartes and even some of the ingenious and often underrated observationalist Vieussens. On the ideological side Thomas Soemmering (1755–1830) in spite of fundamental contributions including pictorial masterpieces to brain anatomy "reverted to the mediaeval theory of ventricular function when he contended in 1796 that fluid in the brain ventricles could be animated and was the immediate organ of the soul". His *Über das Organ der Seele* was inspired (though also criticized) by and dedicated to Immanuel Kant ("unserm Kant gewidmet vom Verfasser").

And so we come by way of full and highly interesting chapters on Eastern models and phrenology in its own right to the scientific investigation of cerebral convolutions in the nineteenth century, via Flourens, J. Hughlings Jackson, Fritsch and Hitzig, and the cyto-architects to Penfield's direct cortical stimulation studies and a final extensive assessment of cortical localization today — ending with isotope radioactive brain scanning (illustrated).

Here, then, is a wealth of pictures synoptically integrated with a full historical, medical and artistic discussion. William of Conches's description of the brain (O'Neill, Y. V., *Clio Med.*, **3**, 203 ; 1963), Tiedemann's illustrations of the cortex in negroes (influential in the controversies around the slave trade), Kurt Goldstein's attack on anatomical localization on a broad front against a background of deep insight, neurological as well as general-biological, and the changing experimental techniques from Joh. Gotfried Zinn to W. Feldberg deserve additional attention. Nothing like that, however, can detract from the distinct merit of this most admirable treatment of the subject including the elegant atlas of impressively evocative illustrations.

WALTER PAGEL

Microphysical Phenomena

Quantum Physics and Ordinary Language. By T. Bergstein. Pp. xii + 61. (Macmillan: London and Basingstoke, October 1972.) £3.

QUANTUM theory treats of microphysical, and therefore not directly observable, phenomena. This raises the problem of language and its descriptive powers. We have only two concepts—wave and particle—describing space-time movement as established in classical physics. These concepts must serve for describing the phenomena on the atomic level and below it where, however, they are found to be complementary. The two concepts are mutually exclusive in the sense that they cannot be used in the same descriptive statement without incurring contradiction. They are exhaustive of the universe of discourse since together they suffice to describe all the phenomena that can be observed.

This book deals with the conceptualization of experience as first given by Niels Bohr by his principle of complementarity. Ultimately, all laboratory experiment, whatever its object and however "abstract" the theory on which it is based, must come down to the level of classical physics and ordinary language since the scientist can only read meters and clocks. The fundamental concepts of classical theory, like space, time, and cause, cannot be used without restriction in quantum mechanics. A physical observation implies an action which is an integral multiple of the quantum of action, *h*. The uncertainty principle precludes the use of classical concepts in the quantum domain while we cannot do without them in the laboratory. The situation presents us with an "aporia" as known from standard philosophy. Complementarity overcomes it but at a price: there is an interdependence of phenomenon and concept. The dividing line between phenomenon and instrument, or between object and subject, is movable since no meaning can be assigned to a result apart from the measuring method by which it is obtained.

Objectivity is expressed by the use of ordinary language and of classical physics. If this view is accepted, then there is always a part of experience that cannot be made "objective". The complementarity between observation and definition of an object, or between the definition of a concept and its applicability, makes it impossible to prove the objectivity of ordinary language as a whole. A kind of Gödel inconsistency appears that forces us to accept natural language immediately, at least in part, in order to make science "objective". All the same, complementarity does not limit natural science but, in fact, extends its scope through the movability of the boundaries of the dual concepts.

Much of what is said in this book follows Bohr's original arguments. I wonder whether it is not necessary, after almost fifty years of discussion of the quantum-mechanical principles, to start on a new approach, for example, by means of the concept of information. The very extensive, and often illuminating, literature on the subject is also not considered by the author. This makes the monograph rather less interesting than it might have been.

E. H. Hutten

Basic Thermodynamics

Classical Thermodynamics. By D. Elwell and A. J. Pointon. Pp. 300. (Penguin: Harmondsworth, Middlesex, October 1972.) £4.

This is a good introduction to thermodynamics which deals with the three laws, basic kinetic theory (viscosity is not mentioned) and various applications to phase changes, magnetic and dielectric materials and thermoelectricity. The last part deals with thermal measurements. Students will obtain a good working knowledge of thermodynamics from this book.

There is little departure in the exposition from what may be called the usual treatments. Complications which arise in the proofs of the equivalence of various forms of the third law are not mentioned: in such arguments hypothetical materials should be considered for which the entropy-temperature curve approaches the $T=0$ axis at two separated points, thus ensuring unattainability of the absolute zero without providing a unique entropy value at $T=0$. Also, the one-page exposition of Carathéodory's principle is somewhat confused, and ought to have been omitted. The statement here that states which are adiabatically accessible from a given state "are limited to a surface in (P,T,v)-space" is false, and encourages confusion (which I believe is still too widespread) between an adiabatic change and an isentropic or quasistatic adiabatic change. But these are marginal points of criticism of an otherwise useful exposition.

P. T. Landsberg

Brain Nutrition

Lipids, Malnutrition and the Developing Brain. (A Ciba Foundation Symposium jointly with the Nestlé Foundation in Memory of Sir Norman Wright.) Pp. viii+326. (Elsevier/Excerpta Medica/North Holland: Amsterdam, London and New York, 1972.) Dfl. 40; £4.80; $12.50.

As a general rule the published versions of the symposia of the Ciba Foundation are valuable additions to most libraries and this volume is no exception. It is well produced, illustrated and indexed, and the editors have almost captured the atmosphere that these small and usually productive symposia generate.

The topic of the symposium is one of vital interest not only from the scientific point of view but also because of the far-reaching implications that the experimental work with animals and the observations on malnourished children have for mankind in general.

While it is true that some of the material in the volume can be gleaned from the literature its assembly in one volume is useful. The discussions following each paper which are also included, as is the custom, give the main participants the opportunity of expanding their ideas in a slightly less formal way than in their papers.

The symposium covered a wide field but one major theme and two related themes were dominant. The first concerned the implications of the timing of malnutrition in relation to the chronological development of the brain.

The two other themes were related to the first but deal in greater detail with the biochemical changes associated with dietary treatments on the processes of myelination, and more especially with the effects of essential fatty acid intake on the formation of brain lipids, including those involved in myelin formation. All the contributions in these areas show how the complex chemistry of the brain lipids is yielding a rich harvest for the biochemist and biophysicist.

The papers given at this symposium show that knowledge of the basic biochemistry of brain tissue is advancing rapidly, but that the changes produced by malnutrition cannot yet be related to the functional properties of the brain.

The two papers concentrating on behaviour emphasize the difficulties involved in relating the biochemical effects of malnutrition with behaviour both from the conceptual viewpoint and also when one attempts to apply them to man where cultural effects further confuse the issue.

This in no way implies that the tone of the symposium is negative; it is extremely provoking in pointing to the difficult areas which remain to be explored.

One is left with the feeling that the "extra-curricular" discussions at this symposium must have been exciting and stimulating for researchers in this field, and that for the non-participant this volume represents the next best thing to having been there.

D. A. T. Southgate

The Evolving Brain

The Brain in Hominid Evolution. By Phillip V. Tobias. Pp. xv+170. (Columbia University: New York and London, February 1972.) £4.75.

This book, based on the author's 1969 James Arthur Lecture on the evolution of the human brain, is surely the most complete and up-to-date compilation of the volumetric data of the brain casts of fossil man and the extant pongids. Tobias, perhaps wisely, has not ventured into the difficult, if not dubious, study of cerebral morphology guessed from plaster endocasts, nor has he pursued any substantive questions of comparative neuroanatomy, beyond the most cursory examination of variables such as neurone number, size, density, dendritic branching, and glial/neural ratios. The main parameter discussed is that of brain size, as reflected by the volumetric capacity of endocasts.

The first six chapters are a compilation of data existing for living primates and the fossil hominids. Some of the data, particularly of the East African hominids from Olduvai Gorge, are previously unpublished. The last five chapters deal with the problem of interpreting the 1,000 ml. growth in brain size during hominid evolution, particularly in terms of primate problem solving abilities, and the prehistoric artefacts associated with the hominids. Throughout, this book is written clearly, even delightfully, and the ample tables, illustrations, and photographs are certainly first-rate, a tribute to Tobias's colleagues, particularly Alun Hughes, who helped in the preparation of this book. The only outright error I could find in this book was a reference to one of my own publications (1969a, "the role of the brain in human mosaic evolution", which through some strange chain of events was never actually published in the *Eighth International Congress of Anthropological and Ethnological Sciences,* Tokyo, 1968). Thus the reference should read "unpublished manuscript", but that is not Tobias's fault.

The evolutionary picture that Tobias draws, on the basis of the few endocranial remains of the hominids thus far discovered, is one of a fairly singular and almost constant advance of cranial capacity and cultural complexity (based on stone tools), from an unknown size of *Ramapithecus* to *Australopithecus* to *Homo habilis* to *Homo erectus*, and so forth. This picture is surely oversimplified, for it excludes any dynamism or change of selection pressures beyond that associated with cultural complexity. Unfortunately, the major component of a cultural adaptation, namely the use of arbitrary symbols or symbolization, is never explained in any neural terms. Indeed, the whole issue of selection for body size and allometric growth of the brain is ignored, except in relation to Tobias's continuing use of Jerison's concepts of the "extra neurones" in the cortex, which are produced in tables for the hominids, including the East African *habilines*. This is not really a criticism, however, for the problem eludes all of us, and the book retains a clarity that would have otherwise been lost if this consideration had entered the discussion.

I am naturally gratified to find my own name and works so often referenced. I am curious, however, why Tobias continues to use a value of 500 ml. for the Taung specimen, when both he and Alun Hughes corroborated my results of 442 ml. for the adult, based on a value of 405 ml. for the child. All three of us found that my midline was accurately placed within one millimetre. I also must demur regarding any "chicken-egg" argument with Washburn over the role of the brain in human mosaic evolution, as I only pointed out that reorganization of the brain along human lines had taken place very early in human evolution, which is not the same as saying "the brain evolved first". Both Bielicki's (1969) and my (1967) papers, utilizing Maruyama's discussion of deviation-amplification and feedback between brain and cultural evolution, form the basis for the synthesis that Tobias attempts to bring forth near the end of the book; but why did Tobias not find my original synthesis between brain size, internal cortical structure, and the evolution of behaviour of some use, beyond a general citation?

The volume has much to present in exemplary fashion, but one cannot help feeling that the interpretative task still remains to be worked out, and that it is this aspect of the book which is perhaps a little weak. For example, Tobias offers the following schema for parameter interrelationships: increase in brain size⇄increase in complexity of internal organization⇄changing functional patterns⇄changing patterns of behaviour. Unfortunately, this model is only partially discussed, and one is left with the impression that Tobias indeed sees the first and last items as ends of a chain. Is this possible, or should it really be a continuous cycle of interrelatedness without ends? Certainly these two "ends" of the chain should be studied.

While this book by Tobias is an admirable and much needed compilation of recent data and perspectives on the evolution of the human brain, the serious student should closely examine many of the references given for himself, and should remain sceptical of several of the values given for the East and South African hominids, regardless of who did the determinations. This latter *caveat* is most important because the methods of ascertaining the volumes, particularly those based on partial endocasts, have not yet been fully tested for their accuracy. This is particularly applicable to the Olduvai Hominid 16, and to some of the South African fragments, such as MLD37/38 and STS 19/58.

R. L. HOLLOWAY

Algebraic Geometry

Introduction to Algebraic Geometry. By Serge Lang. Pp. xi+260. (Addison–Wesley: Reading, Massachusetts, 1972.)

THIS is an unchanged reprint of the book with the same title first published by Interscience in 1958. It gives an introduction to algebraic geometry, including the following topics: Places, algebraic sets, *k*-varieties, (affine, projective, abstract) varieties, Zariski topology, correspondences, product varieties, derived normal varieties, linear systems of divisors, differential forms, simple points, algebraic groups, Riemann–Roch theorem on curves.

This book does not cover the intersection theory, Grassman varieties, Chow varieties nor equivalence relations of cycles.

Chapter I contains basic theorems on valuation rings. Chapter II deals with algebraic sets, *k*-varieties and product varieties. Chapter III introduces the Zariski topology. Chapter IV considers geometric correspondences and the notion of abstract variety. Chapter V contains Zariski's main theorem for birational correspondences. Divisors and linear systems of divisors are dealt with in Chapter VI. Chapter VII deals with differential forms, Chapter VIII with simple points and Chapter IX with algebraic groups and abelian varieties. The Riemann–Roch theorem on algebraic curves is proved in Chapter X. Most chapters contain some useful references to literature. The book could well be used for a specialist course on algebraic geometry at the final honours or at postgraduate level.

T. J. WILLMORE

Keratins

Keratins: Their Composition, Structure and Biosynthesis. By R. D. B. Fraser, T. P. MacRae and G. E. Rodgers. Pp. xi+304. (Charles C. Thomas: Springfield, Illinois, June 1972.) $16.75.

THE keratins are the α-keratins of mammalian epidermal appendages—hair, wool, horn and hoof and the feather keratin of birds and reptilian skin. They have played a central part as a material around which many of the key concepts in structural molecular biology have developed and are of more than academic significance to dermatologists, cosmeticians and, fortunately, the Australian wool industry. Part of the interest of this book is that it is essentially a product of the Division of Protein Chemistry of the CSIRO in Melbourne, a laboratory which has been largely responsible for modern views on the structure, composition and biosynthesis of keratins.

This volume reviews several aspects of the keratins. The histology and fine structure, the molecular structure and arrangement within the keratinized tissue, the physical properties and chemistry of the keratins are all described. There is an admirable didactic chapter on biosynthesis and a tantalizing concluding account of our woefully restricted understanding of the evolution of the keratins. The complexity of keratin structure is astonishing in view of their relatively inert biological function, and there are some suggestions in the book as to the reason for this.

This book fills the need for a comprehensive source-book on the keratins. The relevant data and arguments are presented and, in controversial situations a reasoned assessment provided. The production of figures and photographs is excellent.

ANDREW MILLER

Geography of Disease

Man, Environment and Disease in Britain: a Medical Geography through the Ages. By G. Melvyn Howe. Pp. xviii+285. (David and Charles: Newton Abbot, Devon, September 1972.) £4.75.

IN a way, this volume may be regarded as an extension of the author's previous book, the *National Atlas of Disease Mortality in Britain*. Here, in fact, Professor Howe sets out to look a little more closely at some of the variation charted in his atlas, and to attempt to compare the geographical variation with other differences of a biological, cultural and geological nature. He is also well aware that the dimension of time cannot be ignored in such studies, and looks at population history as well as the comings and goings of various diseases in the past.

The text is liberally supplied with illustrations, usually in the form of schematic maps of the British Isles to show differences as regards such variables as temperature, rainfall, blood groups, mineral and water differences, pollution and industry and various diseases. These are certainly essential to a full appreciation of the points made in the text, and allow a brevity of comment which would otherwise not have been possible.

Mention should be made of one small error which could nevertheless give rather a wrong impression as regards the history of the treponematoses in Europe. In Plate 2, two views are shown of a skull from Spitalfields, in London, showing an advanced and extensive osteitis which could well be indicative of some form of treponematosis. But the date is not Saxon as indicated, and although there is still some debate as to whether it could even be pre-Saxon, it is far more likely to be Mediaeval in period. By a slip of the pen, it has also been attributed to the British Museum of Natural History, whereas in fact it is in the collection of the Department of Physical Anthropology in Cambridge University. Contrary, then, to what this specimen might seem to indicate, there is no certain case of treponematosis in Britain before late Mediaeval times.

All in all, this is a welcome addition to the geography of disease, and simultaneously is a contribution to human ecology and the history of medicine. Moreover, as a reference work, it will be useful to all those concerned with the reasons for biological variation in man.

DON BROTHWELL

Muscle Physiology

Electrogenesis and Contractility in Skeletal Muscle Cells. By J. Zachar. Pp. 638. (University Park: Baltimore, Md. and London; House of the Slovak Academy of Sciences: Bratislava, March 1972.) $28.50.

DR ZACHAR makes for this book the modest claim that it is "intended for workers beginning in the field of general physiology of muscle contraction", and that for workers in other areas of physiology it "serves as a review of the present-day state of knowledge of electrogenesis and contractility of skeletal muscle". The first section of the book, dealing with the "molecular basis of contraction", achieves these aims in a satisfactory way, but this material is already familiar from many books and reviews, and the treatment does not go beyond the level that the reader has been led to expect. Things change, however, when the author gets on to his own ground, namely the electrical behaviour of the membrane systems of muscle, and excitation-contraction coupling. Here each topic is dealt with thoroughly: theoretical treatment, historical background, and a summary and review of almost all of the recent papers are combined in a consecutive and readable text. All points of view are given a hearing, but Dr Zachar's judgment is always sound. Much quantitative material is collected from scattered sources into the thirty-seven tables which accompany the text. Key illustrations are reproduced from many papers. The book restricts itself to striated muscle; the emphasis is on single-fibre experiments, and as a result the great majority of the material is from the frog and from various crustaceans. Within this scope, very little is missed, as is suggested by the fact that the list of references runs to 1,200 items—complete with titles and final as well as initial page numbers. There are both author and subject indexes.

These features make the book a first-rate guide to the literature of membrane properties and excitation-contraction coupling in striated muscle. As such, it will be valuable not only to those who are starting out on research, but also to established workers in the muscle field. I doubt whether there are even any specialists who know the literature so well that they would not find this book valuable, especially because it contains numerous references to papers in Czech and other Eastern European journals that are not well known in the West, and because it contains a fair amount of unpublished work from the Zachars' laboratory. For the beginner, and for the worker on other aspects of muscle, it will be invaluable. It is perhaps more detailed than is necessary in a review of present-day knowledge for biologists outside the muscle field.

According to the preface, the typescript was submitted for publication in 1968, and it is unfortunate that the book did not appear (at least in Britain) until the summer of 1972 (although it is dated 1971). Additions were, however, made in proof, and it is greatly to Dr Zachar's credit that the book does not now give the impression of being out of date. Its value will indeed increase as the years go by and reviewers concentrate on later material; much of the great quantity of experimental work of the 1960s and late 1950s that is brought together here would be lost if it were not for the service that Dr Zachar has done in writing this book.

A. F. HUXLEY

Volcanoes

Volcanoes. By Gordon A. MacDonald. Pp. xii+510. (Prentice-Hall: Englewood Cliffs, New Jersey, 1972.)

IN my opinion this is unquestionably the best descriptive book on the market about volcanoes. The author, who has himself contributed much to the progress of volcanology, has now succeeded, as few can, in making a serious book so readable that even the non-specialist can profit from and enjoy it. The book opens with personal reminiscences about two volcanic eruptions, and this is followed by an introduction to volcanoes and to the properties of magmas, the raw materials, so to speak, of volcanoes. The next 130 pages contain a well-written descriptive survey of the different products of volcanic action, namely lava extrusions and fragmental rocks of various kinds. A broad survey then follows of the types of volcanoes and their eruptions, illustrated by many eyewitness accounts, and a discussion on the subsurface structure of volcanoes, their geographic distribution and tectonic setting, and their effects (both beneficial and otherwise) on man. The book finishes with a catalogue of the 500-odd active volcanoes in the world and an appendix giving a concise summary of the petrology of volcanic rocks. The work is well illustrated, with 150 photographs and 120 maps and line drawings, and the bibliography of some 500 references is well selected and is complete to about the end of 1969.

There are very few errors or misprints but there is one broad criticism which must be made, namely that, in the interests of making the book readable, the content of quantitative volcanology has been reduced to a low level and its place taken by descriptive matter. To give one example, the term "isopach" has been carefully avoided, and although two isopach maps are reproduced no hint is given that such maps constitute one of the most powerful tools for the quantitative study of volcanic products. In short, though the book succeeds in conveying the excitement and drama of volcanic activity, it fails to portray the basis of careful measurements on which the understanding of volcanism must ultimately depend, and it offers no advice on how such measurements can be made. A further mild criticism is that there is nothing new in this book: it is purely a skilfully written review of the literature. Of course such a review must be welcomed in view of the widely scattered nature of volcanological literature and, as a review of the subject, this book is excellent; but it is somewhat of a personal disappointment to find no new ideas expressed, no new ways of looking at volcanoes, with the author "sitting on the fence" about such controversial subjects as the nature and origin of froth flows and tuff lavas.

Despite these criticisms, this book is clearly a "must" for all students of volcanoes and volcanism, and must now be regarded as the standard source book on this subject.

G. P. L. WALKER

Differential Equations

Theory of Partial Differential Equations. By Melvin H. Liebertstein. Pp. xiv+283. (Academic: New York and London, September 1972.) $16.50.

THIS book is intended to provide an introductory account of the theory of partial differential equations for graduate students of engineering, physics, and possibly also applied mathematics. It has been written in four distinct parts. Part I, which comprises five chapters, gives an outline of the classical development of the subject. This ranges from an elementary account of the theory of characteristics and of the classification problem in E^2 to boundary value problems for the Laplace equation and the heat equation. It also contains a chapter sketching the notion of a properly posed problem.

Part II comprises four chapters, giving some results for both linear and nonlinear equations. These include the Riemann method, distortionless transmission line theory, and a helpful introduction to the Cauchy-Kovalevski theorem. Parts III and IV between them contain six short chapters. Potential theory and the Cauchy problem for the wave equation in terms of a retarded potential occupy Part III. Part IV offers a cursory discussion of some more recent ideas: it attempts, in forty-eight pages, to discuss the significance of *a priori* estimates, error bounds in numerical solutions and the existence of L^p weak solutions, while at the same time offering an outline of some functional analysis prerequisites.

Although an attempt to make the theory of partial differential equations better understood by engineers and physicists is to be welcomed, it is very doubtful that this book will be the vehicle by which this is achieved. It is certainly an interesting attempt, but it is too short, too selective, and too uneven in level. Thus on page 12 the reader is expected to know the meaning of the logical conjunction symbol $\wedge$, yet in the previous pages a first year derivation of D'Alembert's solution is offered. This unevenness of presentation mars an expository text, as does the failure to discuss first order systems, the absence of any systematic account of integral equations or of variational methods, and inconsistency of spelling (Kovalevski(y)).

A. JEFFREY

Liquid Metals

Liquid Metals: Chemistry and Physics. Edited by Sylvan Z. Beer. (Monographs and Textbooks in Materials Science.) Pp. x+731. (Marcel Dekker: New York, 1972.) $19.50.

ON page one of this work there appears the remark ". . . physicists and chemists may not be familiar with the formalism commonly used by metallurgists . . . the goal . . . is to outline the formalism and to explain some of its characteristics". This is an excellent spirit in which to start a volume containing review articles by physicists, metallurgists, and chemists written for the benefit of all research workers in the liquid metals field. Let me say at once that the book will be of great value to any laboratory seriously interested in liquid metals, and it is no detraction to add that in any case there is nothing similar available.

The work deals with science, not technology. Fifteen articles, by experts in their fields, span most of the topics one would expect to find. The main emphasis is on comparing observations with theory, but there are substantial sections on experimental techniques and a useful amount of tabulated data. Perhaps the most conspicuous absentee is inelastic neutron scattering and thermal motion but, on the other hand, there are unexpected fringe benefits in the articles on solid non-crystalline alloys and evaporation kinetics.

As a physicist I was grateful for the lucid introduction to metallurgical thermodynamics in chapter 1, and metallurgists and chemists should be correspondingly pleased with the excellent articles on optical, magnetic and electronic properties. Most of the equations one is likely to want in diffraction analysis are set out by Wagner who deals extensively with multi-component systems and with technical questions like error analysis. Very readable chapters are available on viscosity, diffusion, and on electro migration—a subject "once considered mysterious" as the author puts it. The varied fortunes of significant structure theory applied to liquid metal properties are illustrated by Breitling and Eyring while Lee and Lichter attempt to relate thermodynamic properties with electron transport in alloys—an ambitious effort not wholly convincing to me. Sound propagation, high pressure effects and surface tension are the remaining subjects, all providing much of interest.

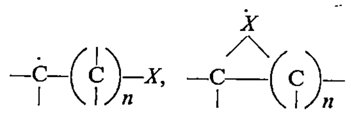
The printing and presentation are clear and the separate systems index is a useful feature. The book needs two complements: an expository textbook conceived as a whole and displaying the subject logically, and a collection of more recent material from the past two years. The recent book by Faber, reviewed elsewhere, promises to supply the first, and before long the Proceedings of the Second International Conference on Liquid Metals will supply the second. Since the subject appears to be on a somewhat gently rising plateau of achievement at present, all these three different volumes promise to be useful for several years at least.

N. E. CUSACK

Radical Intermediates

Bridged Free Radicals. By Leonard Kaplan. Pp. xv+481. (Marcel Dekker: New York, September 1972.) $24.50.

THE subject of bridging in free radicals [that is, the relative importance of the radicals



and radicals intermediate between them] has to be considered when rationalizing product distribution, kinetics, energetics, and spectra from many free radical reactions. Currently (see *J. Amer. Chem. Soc.*, **94**, 6550; 1972) the importance of bridged radical intermediates continues to be subject to much controversy.

A large quantity of information relevant to the subject of bridged radicals is buried in the literature, and this book intended as a comprehensive source for reference and teaching is to be welcomed. The various definitions of bridged radicals are critically discussed, and the book has chapters on silyl-, germyl-, stannyl-, chloro-, bromo-, iodo-, sulphur-, cyano-, and vinyl-substituted radicals. Selected data relevant to particular bridged radicals are briefly and sometimes critically discussed, and the inclusion of comprehensive tables, with extensive footnotes, makes it possible for the reader to draw his own conclusions, as is the intention of the author. This may be possible for readers expert in free radical chemistry, kinetics, stereochemistry, thermodynamics and spectroscopy; however, a person requiring to know if a particular radical is likely to be bridged may be overwhelmed by the welter of tabulated experimental results on which much effort must be expended to arrive at a meaningful conclusion. The mass of detailed tables, the continual necessity to refer to footnotes and to earlier sections, make the book difficult to read. In my opinion the book will be primarily of value to the expert in the field of bridged free radicals. The non-expert, be he teacher or student, may well be baffled by the scarcity of summaries and definitive conclusions.

D. I. DAVIES

CORRESPONDENCE

DDT and Pelicans

Sir,—*Nature* (**240**, 248; 1972) reports Dr Robert Risebrough's allegation that reproductive failure of the brown pelican in 1969-72 on Anacapa Island was due to DDT pollution "from a Los Angeles factory which in 1970 was discharging 500–1,000 lb of DDT daily into the sea".

This is a charge that Dr Risebrough has been making against Montrose, the factory he is referring to, for the last two years. I have sent letters to a California legislative committee and to Dr Risebrough himself outlining Montrose's treatment of its effluent since its start of manufacture more than 25 years ago. We have always settled DDT effluents in a settling pond, hauling the DDT sediments to a dump that accepts such wastes once or twice a year. The effluent to the county sewer line has contained entrained DDT equivalent to about 10–15 pounds per day. In May 1971, Montrose achieved essentially total recycle of its wastes and its discharge is about 1 oz of DDT per day.

The discovery of brown pelican reproductive failure was made shortly after the large oil-spill at Anacapa in 1969. W. Hazeltine (*Nature*, **239**, 410; 1972) and Switzer and Wolfe (*Nature*, **240**, 162; 1972) point out the invalidity of the attempted correlation of DDE residues and eggshell thinning.

At recent Washington DC DDT hearings, cross-examination of Dr Risebrough and others who hold to this correlation theory clearly demonstrated that without exception they used unreliable statistical approaches. Others, who have applied valid statistical analysis, such as Switzer for terns, demonstrated no such correlation.

Dr Risebrough's charges are becoming entrenched in the scientific literature. When such charges are referenced often enough, they become irrefutable "facts". I would hope that *Nature* will not allow itself to become part of this process.

Yours faithfully,
Max Sobelman

Montrose Chemical Corporation,
Torrance, California 90507

Creation in California

Sir,—Although I hesitate to claim to be an expert "in a field of science bearing on the evolutionary theme", and therefore have not been able to take up your offer (*Nature*, **239**, 420; 1972), I have recently been involved in teaching and research on chemical taxonomy, and this has enabled me to look afresh at the subject of evolution. This has been done against a background of work on biogenesis which has certain similarities to evolution, for in it an attempt is made to determine how simple molecules have evolved into more complex ones during the life of the plant. Fifty years ago phytochemists speculated on possible pathways of biogenesis, some most fruitfully, but no one accepted these ideas as fact (or "truth") till innumerable experiments, checking and rechecking claims, have established some pathways with reasonable certainty. Looking therefore afresh at evolution, the most striking feature I find is the highly speculative nature of the topic; the situation phytochemists (in their obviously much more limited sphere of interest) were in 50 years ago.

For instance, one would have expected that classification of plants and animals would have been one of the first subjects to benefit from Darwin's ideas, as here at last was the basis for a "natural classification". Some modern plant taxonomists do not agree and feel that nothing has been fundamentally effected. "What is the impact of Darwin's ideas on taxonomy? It is commonly stated, or implied, that they were revolutionary. No taxonomist who has ever given a moment's thought to what he is doing in comparison to his predecessors can believe this. He knows that taxonomy in its broad outlines and in its more detailed practice has hardly been affected by evolutionary ideas. There is a curious dishonesty about this in much biological writing. Either the fact is denied, or it is glossed over, as if it is something to be ashamed of"[1]. In fact some seem to suggest that evolutionary ideas have been a hindrance to taxonomy. "In the absence of complete fossil records, so-called 'phylogony' is deduced from taxonomy. Attempts to base taxonomy on 'phylogenetic criteria' generally involve circular arguments, and it is now belatedly coming to be realized that evolutionary speculation has had a deleterious effect on practical taxonomy"[2]. I find it difficult therefore to accept your opinion that "Darwinism occupies a place in science at least as strong as that of Newton's Laws".

Clearly, the situation is no fault of the biologists; if adequate facts are not available they have to do with what they have. But it amazes me why biologists seem wedded to the rather limiting assumption that God must have created life only once. Could He not have repeated the operation, on various scales of complexity, several times, thus explaining the great gaps between phyla and such insoluble problems as the origin of the angiosperms? I should guess that one of the motives behind the "Californian Creationists" is to ensure that young people are aware that the Bible, *inter alia*, at least suggests this possibility. Like many of the people referred to by Dr Hayward[3] I treat the Genesis account of creation with as much respect as that of the biologist. Perhaps we are not too far removed from Darwin, who ended his *Origin of Species* with these words: "There is a grandeur in this view of life, with its several powers, having been originally breathed by the Creator into a few forms or into one whilst this planet has gone cycling on according to the fixed law of gravity. . . ."

Yours faithfully,
J. W. Fairbairn

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University of London,
29/39 Brunswick Square,
London WC1N 1AX

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[1] Walton, S. M., in *Chemical Plant Taxonomy* (edit. by Swain, T.), 6 (Academic Press, London and New York, 1963).

[2] Watson, L., Williams, W. T., and Lance, G. N., *J. Linn. Soc.*, **59**, 492 (1966).

[3] Hayward, A. T. J., *Nature*, **240**, 577 (1972).

Doctrine of Creation

Sir,—The argument as between the theory of evolution in general and Darwin's theory of natural selection in particular on the one hand, and the account of the creation in the book of Genesis on the other, is surely of no religious interest. But that such an argument should exist is of profound significance for science.

All scientists know that it is not the purpose of science to arrive at ultimate truth. Science is nothing more than a systematic description of phenomena by means of "theories", commonly expressed in the form of "laws". None of these theories and laws is sacrosanct: all are provisional.

As a small boy, early in the century, I was brought up in an old-fashioned school. We were taught that the biblical story of the creation and the subsequent events in the garden of Eden was an allegory. The allegorical truth of that story still remains unshaken. That is so in spite of the fact that I sometimes feel I can detect certain ideological overtones in the writing.

That scientists should still be arguing

about these things is saddening. It betrays a pathetic lack of scientific faith[1].

Yours faithfully,

V. B. WIGGLESWORTH

Gonville and Caius College,
Cambridge

[1] Wigglesworth, V. B., *Ann. Appl. Biol.*, **60**, 1 (1967).

Noah's Haemoglobin

SIR, — In the ecumenical interest (*Nature*, **239**, 420; 1972), we wish to point out that the latter portion of Genesis is consistent with current theory of molecular evolution.

Kimura (*Nature*, **217**, 624; 1968) and King and Jukes (*Science*, **164**, 788; 1969) propose that protein evolution has occurred mainly through neutral mutations which have no effect on molecular function and no selective advantage. Haigh and Maynard Smith (*Genet. Res.*, **19**, 73; 1972) have examined this theory with respect to the published data on human haemoglobin variation. They conclude that if the theory is correct the human population must have passed through a period of drastically reduced size prior to the more recent rapid population increase. The population bottleneck is necessary to give initial genetic homogeneity, a requirement for agreement of theory and observation.

Genesis, chapter 6, contains a full description of events causing a reduction in the human population to eight individuals; Noah, his wife, their three sons, Shem, Ham and Japheth, and the sons' wives. It seems entirely plausible that this small population could be homogeneous for haemoglobin genes. Thus the book of Genesis documents a series of human population changes which are consistent with changes required from consideration of amino-acid sequences alone.

Yours faithfully,

RICHARD N. HARKINS
PETER STENZEL
JOHN A. BLACK

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Division of Medical Genetics,
University of Oregon Medical School,
Portland, Oregon 97201

Titles and Reprints

SIR,—As a librarian, I can easily answer the puzzle postulated by Briggs and Briggs[1] as to why more requests were received for a paper published in *Contraception*[2] than for the one in *Nature*[3]. *Nature* is more readily available. Virtually all scientific libraries have at least one subscription to *Nature*; whereas relatively few subscribe to the highly specialized *Contraception*.

Even though photocopying is cheaper than mailing a request, without the journal at hand a reprint is necessary.

Also as a librarian, I want to admonish the editor of *Nature* for publishing a paper with a deliberately misleading title. This paper will turn up as a false drop for years to come. The use of titles has become a powerful literature searching technique[4]. It is bad enough that uninformative titles are still being written through ignorance, but to write phoney titles intentionally is just outright perverse.

Yours faithfully,

DONALD A. WINDSOR

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SciAesthetics Institute,
Post Office Box 604,
Norwich, New York 13815

[1] Briggs, M. H., and Briggs, M., *Nature*, **240**, 490 (1972).

[2] Briggs, M. H., Briggs, M., and Austin, J., *Nature*, **232**, 480 (1971).

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Announcements

University News

Dr William Robert Dearman, Newcastle upon Tyne, has been appointed to a professorship in engineering geology from August 1, 1972.

Dr Alan Williams, Leeds University, has been appointed Livesey professor and head of the Department of Fuel and Combustion Science from January 1, 1973.

Dr G. C. Morrison, Illinois, USA, has been appointed to the Chair of Nuclear Structure at the University of Birmingham.

Professor Roger Penrose, Birkbeck College, London, has been appointed to the Rouse Ball Professorship of Mathematics, at the University of Oxford, in succession to Professor C. A. Coulson, Oxford.

Appointments

Dr Edwin Clarke, MD, FRCP, has been appointed Director of the Wellcome Institute of the History of Medicine as from October 1, 1973.

Miscellaneous

The **Lomonsov Gold Medals for 1972**—the highest award of the Soviet Academy of Sciences, awarded annually for outstanding achievements in the natural sciences to one Soviet and one foreign scientist—have been awarded to **Academician Nikolsi Ivanovich Muskhelishvili** for his work in mathematics and mechanics, and to **Professor Max Steenbeck** (German Democratic Republic) for his research on plasma physics.

Professor Arpad I. Csapo, Washington University, has been awarded the 1972 award of the **International Health Foundation** on "Prospects for Practical Application of Prostaglandins".

International Meetings

The University of Texas Health Science Center, Houston, announces the Tenth Symposium on Biomathematics and Computer Science in the Life Sciences to be presented at Houston, Texas, March 1973. (Dr Stuart Zimmerman, University of Texas.)

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Agricultural Research Institute of Northern Ireland. Forty-fifth Annual Report, 1971/1972. Pp. 43. (Hillsborough, Co. Down: Agricultural Research Institute of Northern Ireland, 1972.) [2910

Towards a Future for Inland Shipping. (Comments by the Inland Waterways Association on the Future of Inland Waterways Transport in the Light of the Proposed Regional Water Authorities.) Pp. 12. (London: The Inland Waterways Association, 1972.) 20p. [2910

Bulletin of the British Museum (Natural History), Entomology. Vol. 27, No. 5: On European Pteromalidae (Hymenoptera): a Revision of *Cleonymus*, *Eunotus* and *Spaniopus*, with Descriptions of New Genera and Species. By Z. Boucek. Pp. 265–315. £1.85. Historical Series. Vol. 4, No. 3: Charles Darwin's *Queries About Expression*. By Richard Broke Freeman and Peter Jack Gautrey. Pp. 205–219+1 plate. 65p. Zoology. Vol. 23, No. 1: The Gunong Benom Expedition 1967. 1: Introduction. By Lord Medway. Pp. 1–7+4 plates. 75p. Vol. 23, No. 2: The Gunong Benom Expedition 1967. 2: An Outline Description of the Forest Zones on North-East Gunong Benom. By T. C. Whitmore. 3: Bryophytes and Filmy Ferns from Gunong Benom. By Anne Johnson. Pp. 9–20+8 plates. £1.15. Vol. 23, No. 4: The Gunong Benom Expedition 1967. 5: Reptiles and Amphibians of Gunong Benom with a Description of a New Species of *Macrocalamus*. By A. G. C. Grandison. Pp. 43–101. £2.55. Vol. 23, No. 7: The Gunong Benom Expedition 1967. 8: Ticks (Ixodidae) of Gunong Benom and Their Altitudinal Distribution, Hosts and Medical Relationships. By H. Hoogstraal, B. L. Lim, M. Nadchatram and G. Anastos. Pp. 165–186. 75p. Vol. 23, No. 8: The Gunong Benom Expedition 1967. 9: A Collection of Chiggers from Gunong Benom (Prostigmata: Trombiculidae). By M. Nadchatram. 10: Phthiraptera (Insecta) Chewing and Sucking Lice. By Theresa Clay. Pp. 187–200. 65p. (London: British Museum (Natural History), 1972.) [2910

Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 273, No. 1233: Dynamics of the Liquid Core of the Earth. By C. L. Pekeris and Y. Accad. Pp. 237–260. (London: The Royal Society, 1972.) 65p; $1.80. [2910

BBC Handbook 1973. Pp. 294+75 photographs. (London: BBC, 1972.) 75p. [3110

Imperial College. Royal School of Mines Research Report 1969–72. (Geology, Mining and Mineral Technology, Metallurgy.) Pp. 64. (London: Imperial College of Science and Technology, 1972.) [3110

Procter and Gamble Limited. Annual Report for the year ended 30th June, 1972. Pp. 12. (Gosforth, Newcastle upon Tyne: Procter and Gamble, Ltd., 1972.) [3110

Post Office Investment for the Future. Pp. 24. (London: Post Office, 1972.) [311

Geological Society of London. Special Report No. 2: A Correlation of Cambrian Rocks in the British Isles. By John Watson Cowie, Adrian Williams, Amsler Rushton and Cyril James Stubblefield. Pp. 42. £1.20; $3. Special Report No. 3: A Correlation of Ordovician Rocks in the British Isles. By A. Williams, I. Strachan, D. A. Bassett, W. T. Dean, J. K. Ingham, A. D. Wright and H. B. Whittington. Pp. 74. £1.20; $3. (Edinburgh: Scottish Academic Press, Ltd., 1972.) [311

Forestry Commission. Research and Development Papers. No. 87: Production and Use of Ball-rooted Planting Stock in Sweden and Finland. By A. J. Low and R. M. Brown. Pp. 25. No. 88: Dissemination and Application of Research Information in the Field. By O. N. Blatchford. Pp. 4. No. 89: Formulation and Implementation of Forest

Policy. By D. R. Johnston. Pp. 8. No. 90: Planning and Development of Markets for Man-Made Forests. By F. C. Hummel and J. L. Davidson. Pp. 9. No. 91: Silviculture and Good Landscapes in British Forestry: The Improvement of Planning and Practice. By M. H. Orrom and A. F. Mitchell. Pp. 9. No. 92: The Special Contribution of Forests and Woodlands to Recreation in an Industrial Society. By J. A. Spencer and R. M. Sidaway. Pp. 9. No. 93: Valuation of Non-Wood Benefits. By A. J. Grayson. Pp. 10. (London: Forestry Commission, 1972.) [611

National Coal Board. Mining Research and Development Establishment—Some Questions and Answers and a Brief Account of Its Work. Pp. 14. (Stanhope Bretby, Burton-on-Trent: NCB, Mining Research and Development Establishment, 1972.) [611

Growing Up. By Professor D. G. Walker. (An Inaugural Lecture delivered in the University of Birmingham on May 11, 1972.) Pp. 19. (Birmingham: The University, 1972.) 25p. [611

Forestry Commission. Forest Record No. 83: The Pine Shoot Moth and Related Species. By T. M. Scott. Pp. 14. Forest Commission Bulletin No. 43: Nursery Practice. By J. R. Aldhous. Pp. viii+184+31 plates. £1.50. (London: HMSO, 1972.) [611

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Mineral Resources Consultative Committee. Mineral Dossier No. 3: Fuller's Earth. Compiled by D. E. Highley. Pp. vii+26. (London: HMSO, 1972.) 42p net. [711

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University Grants Committee. First Employment of University Graduates, 1970/1971. Pp. 53. (London: HMSO, 1972.) 75p net. [1411

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The Arts Council of Great Britain. Twenty-seventh Annual Report and Accounts, 1971/1972. Pp. 127. (London: The Arts Council of Great Britain, 1972.) 50p. [1711

Wildlife Conservation and Dead Wood. By Alan E. Stubbs. (Supplement to the Journal of the Devon Trust for Nature Conservation.) Pp. 18. (Exeter: The Devon Trust for Nature Conservation, 1972.) 20p. [1711

Memoirs of the Royal Astronomical Society. Vol. 77, Part 2: The Abundances of the Elements in the Oldest Disk Stars. By J. B. Hearnshaw. Pp. 55–108. Vol. 77, Part 3: Observations of Extragalactic Variable Sources at 2–8 and 4–5 cm Wavelength. By W. J. Medd, B. H. Andrew, G. A. Harvey and J. L. Locke. Pp. 109–158. (Oxford and London: Blackwell Scientific Publications, 1972. Published for the Royal Astronomical Society.) [1711

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The Power of the Purse in the European Communities. By David Coombes, assisted by Ilka Wiebecke. (European Series, No. 20.) Pp. 103. (London: Chatham House; and PEP, 1972.) £1.25. [2011

Other Countries

Unesco. Technical Papers in Hydrology. No. 11: Teaching Aids in Hydrology. Pp. 64. 16 francs; £1.35: $4. No. 12: Ecology of Water Weeds in the Neotropics: an Ecological Survey of the Aquatic Weeds *Eichhornia crassipeses* and *Salvinia* Species and Their Natural Enemies in the Neotropics. By D. S. Mitchell and P. A. Thomas. Pp. 50. 6 francs; 45p; $1.50. (Paris: Unesco, 1972.) [2610

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Travelling in Towns is Necessary but not Impossible

THE Expenditure Committee of the House of Commons has done a useful if somewhat predictable job in its analysis of the problems of urban transport in British cities, published last week (Second Report from the Expenditure Committee, *Urban Transport Planning*, Vol. I, Report and Appendix, £0.42; Vol. II, Minutes of Evidence, £3.95; Vol. III, Appendices and Index, £0.73; HMSO). Unlike many other committees, the Subcommittee on the Environment and Home Office under Mr James Allason, MP has done a thorough job, collecting evidence not merely from the easily accessible ministries and the interested parties such as the Road Haulage Association, the Royal Automobile Club and even the British Cycling Bureau, but also from the local authorities and publicly supported transport organizations which live in the thick of the urban transport problem. The subcommittee's message is simple and a little stark—public transport must be encouraged, private transport must be discouraged and everybody must plan a little better. But the suggestions for improving public transport which the subcommittee's report puts forward are often imaginative. Only its proposals for restricting private transport sound hackneyed. And perhaps the most serious defect of an otherwise valuable report is that the subcommittee has failed to make a sufficiently tangible connexion between the problems of urban transport and the still larger and more durable problems of city planning.

The problem now confronting many British cities has long been familiar in the United States. Commercial vehicles, publicly owned buses and private cars compete for what road space there may be. The more the traffic grows, the greater is the congestion and the less efficient are the buses. The result is that travellers take to their private automobiles, the bus operators find their revenues dwindling and attempt to balance their books by making fewer journeys, which in turn implies that the service which they offer deteriorates and that increasing proportions of travellers are persuaded to take their cars to work. The result is all too apparent. The number of journeys by public buses in Britain has declined steadily in the past decade, from 13.7 thousand million in 1960 to 9.2 thousand million in 1970, while the average length of a journey has also declined. But the proportion of traffic on urban roads as represented by cars and taxis has similarly increased, by 22 per cent in half a decade. And there is nothing to suggest that these trends will quickly be moderated. To be sure, the statistics which the subcommittee has gathered make no allowance for the extent to which increasing congestion on the roads drives people from buses to the commuter railways, but there is at least a prospect that the major cities of Britain may in the foreseeable future find public buses as much a drain on local taxes and as unsatisfactory as they have become in North America.

The report is full of helpful suggestions for striking a better balance. Special urban routes for buses, or traffic lanes reserved for their use, have obviously an important part to play. So too do schemes for making sure that buses travel more quickly, by giving them bigger engines, and schemes for encouraging a flattening of the peak travel hours by offering employers who ask their people to work eccentric hours a rebate on local taxes—one of the most obvious diseconomies of the present balance between private and public transport is that most people wish to travel in cities at about the same time, which increases congestion and decreases the use which is made of the capital locked up in buses. The subcommittee is also warm in its attitude towards unconventional methods of transport within cities—moving pavements, self-drive taxis and minibuses—but unfortunately indecisive. It would have helped if the subcommittee had been more forceful in urging that theorizing about other people's experiments should be replaced by research and development in Britain on these and other schemes.

By comparison, the argument about the need to restrict private transport on urban roads is dull. The subcommittee rightly says that more study needs to be carried out before it will be possible to implement fanciful schemes such as electronic pricing—a hobbyhorse of the National Roads Laboratory, which would install electrical devices in the roads and taxi-meters actuated by them in private cars so as to measure and to charge for the amount of nuisance caused by private transport in urban centres, a cure well calculated to be less palatable than the disease. Taxing permanent parking spaces in, for example, office buildings, may be sensible. There is less to be said for requiring that parking lots should not offer reduced rates to those who stay for longer periods or even for the restriction of off-street parking—if parking

Editor of *Nature*

MR John Maddox, Editor of *Nature* since February 1966, will relinquish his post in the next few months and not later than June 30. Macmillan Journals Limited made the following announcement earlier this week.

"When John Maddox resigned as Managing Director of Macmillan Journals in June 1972, after what was described at the time as an honest but amicable difference of opinion, Macmillan agreed that he should be free to start an independent publishing organization while remaining Editor of *Nature*. More recently, however, Macmillan has reconsidered this decision, and as a result Mr Maddox will cease to be Editor of *Nature* when a successor is appointed later this year. Mr Maddox intends to remain in journalism and publishing."

spaces are suitably taxed, it is surely for those who pay the taxes to decide how best their investment should be made to work. The subcommittee rightly concludes that parking meters at present constitute a source of irritation, but this is again a reason for thinking that the encouragement of off-street parking would make a better policy. And although pedestrian precincts are delightful for those who want to walk in them, surely there is something to be said for first calculating the cost that will be incurred thereby. And it does not make sense to ask that there should be a moratorium on the construction of urban roads until the Department of the Environment has had a chance to reexamine each one of the schemes on which contracts have not yet been let—that is a prescription for more and not less chaos.

The economic analysis running through the report is patchy. In the past few years, the Department of the Environment has become extremely skilled at carrying out cost/benefit analysis of transport schemes, counting in its calculations the cost of people's time and being prepared to recognize that even schemes which operate at a commercial deficit, the new subway systems in London for example, should be counted as beneficial if the benefits exceed the cost. By this means, the Department of the Environment has apparently been persuaded that electric locomotives are better than diesel locomotives on many of the commuter lines in and out of London and many major cities. The trouble is that the kinds of cost/benefit analysis at present being undertaken are much less sophisticated than they should be. At a time when model-building and computer simulation are so fashionable, it is surprising that the department has not thought of constructing a model of British urban transport that would allow it to predict the consequences for the system as a whole of changes in the parameters which define it. Moreover, the economic analysis is still carried out with averages, yet it must be clearly apparent that many of the characteristics of urban transport are determined by the way in which different people put different values on their time and on travelling to work by car. What British cities, and those elsewhere, now need is some means of allowing those who are prepared to pay the full social cost of travelling in cities to do so, and if this means that more roads must be built, that is what urban authorities must stomach.

The weakest part of the subcommittee's report is, however, its implicit assumption that there is nothing much that can be done to reduce the demand for transport in cities by city planning. This, however, is a shortsighted view. It is true that the fabric of a city cannot be changed overnight, but in the long run, even within a decade or so, it is entirely possible that the need for people to thread their way through the intricate networks of streets by which modern cities are represented could be much diminished. The subcommittee is all for fiscal methods for restricting traffic. Should it not also consider fiscal methods for discouraging housing developments and office buildings which, by their location, are certain to add to the demand for transport? In Britain, where planning regulations are in principle quite strong, it is also entirely within the competence of local authorities to guide the development of cities in ways that will permit the efficient use of methods for the rapid movement of people from place to place. One possible solution to this problem is that of a cellular city, a network of comparatively dense townships connected by fast transport links and separated by open spaces. To fail to recognize that this or similar schemes offer the best permanent solution to the traffic problem is disappointing.

Lame Duck or White Elephant?

THE British and French governments will have only themselves to blame if the potential American customers for the Concorde aircraft fail to take up their options to buy, as now seems possible and even likely. From the beginning, the chief argument against the Concorde project has been economic. In the first place, the commitment of what has turned out to be £1,000 million of research and development expenditure by the French and British governments has been an imprudent use of scarce technical resources (and the fact that the original estimate, in 1962, was that research and development would cost merely £150 million is no excuse). In the second place, it has for several years been plain that the economic case for this particular supersonic aircraft was marginal, to say the best of it. The initial cost of each aircraft is now reckoned to be £23 million, while the passenger load (128 at the most) is so small that the operating costs (making allowance for depreciation) may be twice as great as the cost of carrying a passenger for a mile by the most efficient subsonic aircraft now in service. Especially now that airlines are under increasing pressure to show a profit on their present operations, it is understandable that they should be thinking of cancelling their options to buy Concorde.

What may be called the environmental case against supersonic aircraft is, by comparison, irrelevant. Whatever uncertainties there may be about the long-term effects of large-scale supersonic operations on the stratosphere, nobody would seriously suggest that the moderate fleet of Concordes in prospect even before American airlines began turning sour would have measurable consequences, and although take-off noise and the supersonic boom are potentially serious extra nuisances, there is every likelihood that the operations of supersonic aircraft will be appropriately restricted. Indeed, the likelihood that night-time landings and take-offs will not be permitted will put at risk the hope of the aircraft manufacturers that each Concorde aircraft will be able to make four transatlantic crossings in each day, and thus further jeopardize the economics of Concorde. But in any case, in spite of all the theorizing of the past few years, nobody will dispute that the best way of discovering the environmental hazards of supersonic aircraft is to put a few into service. In this sense, the aircraft constructors can congratulate themselves on having carried out a public service, if at enormous cost to the taxpayers of Britain and France.

The practical question with which the British and French governments will be faced, if indeed American orders for Concorde fail to materialize, is to decide whether the programme of development should be continued and whether manufacture of commercial aircraft should be supported. The first thing to be said is that with a large part of the development cost already spent, there is a good case for completing the work and, in the process, for making a sufficiently close technical study of what has been accomplished to permit a realistic assessment of the potential of supersonic commercial aircraft. Would it be feasible to make aircraft flying at Mach 2 or thereabouts sufficiently commodious to carry an economic payload? Is there a possibility that the range of Mach 2 aircraft should be substantially increased? Is the Concorde a possible starting point for the development of an aircraft flying at Mach 3, where the potential benefits of supersonic flight are greater but where other alloys and configurations may be needed? However much the British and French governments may now think that their fingers have been burned, it would be folly for them to overlook the value of the development work already carried out and paid for.

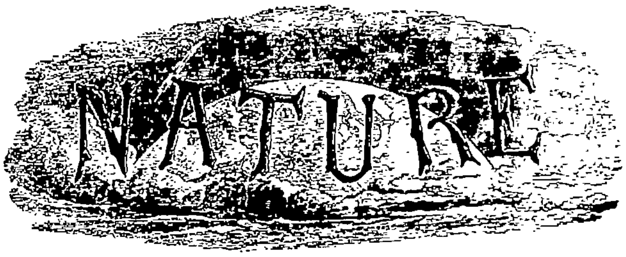
The more difficult question is that of how the aircraft should be brought into commercial service. It will be tempting to suppose that BOAC and Air France should be used as means of demonstrating that Concorde has commercial uses, and to provide the two airlines with a subsidy to keep the aircraft in service for the next few years. This, however, would be a mistaken policy. It is entirely reasonable that the governments should think of writing off the development cost, so that there should be no component of royalty in the price the airlines pay for their aircraft. It is, however, essential that the airlines should not be required to keep on their books uneconomic aircraft which are or become a hidden cost. In the past few months, BOAC, to its credit, has made much of the running in the campaign to bring about reduced fares across the North Atlantic (and it is hoped that the airline will soon extend its fare cutting to other fields). It would be intolerable if the two governments now foisted on their national airlines a scheme for putting Concorde into service which would have the effect of requiring other types of aircraft to shoulder some of the extra cost, for that would imply that ordinary airline passengers would be penalized so as to keep Concorde in the air. If the two governments eventually decide—and there is no reason why they should—that they will put Concorde into service even if the American carriers turn it down, their best course will be to set up a separate operating company, first agreeing to compensate BOAC and Air France for the traffic seduced away from their conventional operations. In such a situation, the true cost of this premature adventure into supersonic flight can be made plain for all to see.

Secrecy in Science

MR AIREY NEAVE, the chairman of the House of Commons Select Committee on Science and Technology, performed an important public service on Monday, first by persuading the House of Commons that it should debate his committee's proposals for administering publicly supported research and development and then by making his own introduction to the debate on attack on the present traditions of secrecy within the government machine. Mr Neave is no doubt still smarting from the refusal of the government to make public the Docksey report on the National Research and Development Corporation, eventually published by the Select Committee itself, and the Vinter report on the future of nuclear power in Britain, still unpublished. But these are only the tips of icebergs. The British government's administration of research and development in Britain is almost exclusively determined by the advice of committees which still operate in confidence and which have the effect not merely of obscuring the reasons why governments make particular decisions but also of preventing those individuals who take part in the advisory process, and who are usually the best informed, from engaging in the kind of public discussion of public issues which might bring enlightenment. Mr Neave is entirely right to emphasize the need for more open discussion.

Mr James Prior, the new Lord President of the Council, had only the weakest of replies on Monday. He held, somewhat implausibly, that it would be impossible to persuade distinguished scientists to give advice at all if they knew that what they said might eventually be published. But might it not be more sensible of him to turn the argument round, and to say that advice which is given only secretly is likely often to be unhelpful and even ill-considered? Worse still, there is of course a danger that if governments like the British neglect to cultivate the scientific community as an important constituent of public life, especially when both the government and the opposition are claiming that steps must be taken to make individuals feel more intimately involved in the making of decisions which affect them directly, the result will be still further to depress their spirits. It is reprehensible that decisions about science and technology should be made behind closed doors.

100 Years Ago



THE NATIONAL HERBARIA MEMORIAL

WE are glad to be able to lay before our readers the reply to the memorial to Mr. Gladstone, signed by so many eminent botanists, which appeared in NATURE for January 16. The answer is in every respect satisfactory :—

"Treasury Chambers, January 23, 1873

"Sir,—The Lords Commissioners of Her Majesty's Treasury have had before them your letter of the 3rd instant, and the Memorial enclosed in it from various gentlemen engaged in the pursuit of botany or in instruction therein, with respect to the transfer to the branch of the British Museum about to be constructed at South Kensington, of the scientific collections and library now existing at the Royal Gardens at Kew.

"Their lordships desire me to request that you will inform the memorialists that Her Majesty's Government have not formed the intention of removing the collection to South Kensington, and that should anything lead them hereafter to entertain the idea, they will take care that ample notice shall be given, and that the judgment of the persons most accomplished in botany shall be fairly weighed in the first instance.

"I am, Sir, your obedient servant,
"WILLIAM LAW

"The Rev. M. J. Berkeley, Sibbertoft,
"Market Harborough"

From Nature, 7, 243, *January* 30, 1873.

OLD WORLD

Water Council Decried

THE National Water Council—the proposed central point of the government's reorganization of the water services in Britain—came under renewed attack last week from the Water Resources Board in its ninth annual report. The bill to bring the changes into effect is due for publication this week.

Since the proposals in December 1971 to merge the twenty-nine existing river authorities and 1,350 drainage and sewerage authorities into ten large Regional Water Authorities, the Water Resources Board has repeatedly approved of the scheme's objects but condemned its methods in that no provision is made for a strong central body to control the activities of the water authorities. The Water Resources Board was one of the first to champion the theory that water services should be dealt with by a few large bodies with wide powers, rather than by many small bodies with limited interests, and Sir William Goode, the board's chairman, reiterates in the report that "this proposal is right and we welcome and support it".

But the board still believes, Sir William says, that a national water authority is needed to formulate and execute national water policy, subject to ministerial direction, to oversee and direct the authorities, to allocate capital investment, to run long-term planning and research and development and to promote major works such as the estuary storage schemes currently under consideration.

At present, the only central body proposed is a National Water Council which "will not in our view be equipped to do what needs to be done at the centre in the coming years".

The National Water Council will have the ten chairmen of the authorities as *ex officio* members and will also have coopted experts, but there are no provisions for an expert permanent staff such as that of the Water Resources Board. A central planning unit will be situated in the Department of the Environment, reporting to the minister and the council, but the Water Resources Board feels that such a unit will have divided loyalties.

The board is also critical of the proposals for the industry's research centre. The centre will not include the Water Pollution Research Laboratory, the only centre in Britain concentrating on water pollution work. The board argues that the laboratory should be involved, together with the existing Water Research Association and with "the relevant parts" of the Water Resources Board. It should be governed and funded by the National Water Council.

But the board's objections are likely to go unheeded with publication of the bill so near. A change of heart at this stage is unlikely.

EURATOM

Decision in February

LAST week's meeting to discuss the European Commission's five year plan for Euratom produced the perennial deadlock that seems to haunt so many European cooperative ventures.

The commission's modified proposals allowed for a cut in the overall budget from 200 million units of account (one unit=one old dollar) to 185 million units and a considerable change in Euratom's hopes for non-nuclear research. Britain, France and the Netherlands, however, would only agree to projects costing 159 million units and the meeting ended unresolved with an agreement to discuss matters again on February 5.

Initial reaction in the commission is one of disappointment. The commission argues that to cut Euratom below the size it proposes will be effectively to close it down. But the British and French reasoning is that Euratom simply needs "pruning", and that cutting it down to the size they propose will not make the organization defunct. Britain is not against providing Euratom with a five year programme (it has existed on a year to year basis since 1968) but feels that those parts of the Euratom programme that have outlived their usefulness should be done away with.

The commission is hopeful, however, that the problem can in fact be settled at a political rather than a technical level. Both Britain and France want the individual projects examined in detail before they commit themselves to expenditure, but the commission, in the person of Mr François-Xavier Ortoli, its president, want the ministers first to accept the need for a common research programme.

One key to the problem is that the Euratom treaty is one of the founding treaties of the Common Market, so that the closure of Euratom would result in the removal of one of the community's *raisons d'être*—a situation that the commission sees as intolerable and which gives it hope that a satisfactory compromise might be reached next month. If Euratom's future has to be sorted out at a purely political level then the commission believes it has a much higher chance of survival.

At last week's meeting Mr Ortoli and Mr Théo Lefevre, the Belgian science minister, both asked the ministers to take a political approach to the problem, pointing out that Euratom's expenditure is only 0.19 per cent of the total that the nine members of the EEC spend on their individual research efforts.

PARLIAMENT

Agreeing to Differ

THE differences of opinion between the government and the Select Committee for Science and Technology were aired once again in the House of Commons on Monday of this week. In a debate which asked the House to take note of the select committee's four reports on research and development and the government's observations on these reports, Mr Airey Neave, chairman of the select committee, called on the government to review its decision not to appoint a minister for research and development.

Mr Neave pointed out that the European Community is seeking a "comprehensive policy on scientific research and technological development". He asked whether the government, if it agrees that there has to be a community policy on research and development, will then consider having a national policy itself.

The government in its white papers turned down the select committee's request for an industrial advisory committee and Mr Neave confessed that he was not clear as to why it had done so. Mr Neave said that the view expressed to the select committee that industry should do all its own research and development is false, and that "a programme of government research and development will have to be maintained by the United Kingdom if it is to remain competitive in the next 25 years".

This suggestion is one of the "main themes behind some of the recommendations of the select committee", said Mr Neave but Mr James Prior, Leader of the House of Commons, said that he was worried that industry had not made full use of all the research which had come from the research councils in the past few years. Mr Prior said that he had been told that if Britain stopped all its research for ten years and merely applied the results of discoveries already made then a high growth rate would still be achieved. Mr Prior did add, however, that he was not advocating this course of action.

UNIVERSITIES

Five Year Plan

UNIVERSITIES will have less to spend on each student during the next five years with the average amount being two per cent down on that spent in 1972–73, according to the University Grants Committee. This is the upshot of the government's plans for education announced in December (*Nature*, **240**, 372 ; 1972).

The money available to universities for each student has increased during each of the last two five-year plans although the estimated ten per cent increase per student planned to occur between 1967 and 1972 only amounted to half this because the number of students increased by more than had been planned.

The UGC in its memorandum released last week offers advice to universities on how the grant for the next five years should be allocated between departments. Although the universities are free to spend the block grant they receive as they choose, the UGC hopes that the guidelines it proposes will be adhered to.

The committee recommends that during the next five years, universities should allocate their grants according to Table 1 which is assessed on the basis that the average for the different subjects is 98 per cent of that spent at present.

The UGC stresses that all universities will not have to decrease their spending by two per cent per student and that some will therefore have to decrease spending by more than this. The committee points out that medical schools are in a state of rapid development caused especially by Lord Todd's report on medical schools in London, published in the late 1960s. The UGC states that clinical medical departments outside London should be able to develop with the same level of support as they now enjoy.

The committee says that the recommended relative rates of spending shown in Table 1 have been arrived at by considering the "present pressures on the different disciplines and the way in which growth to 1976–77 will affect them". The fact that pressure in recent years has been on arts places rather than science made the government decide in the education white paper that the present ratio of arts to science of 45/55 be changed to 47/53 by 1976–77. Thus, says the committee, "it would appear that the room for economies of scale as growth proceeds are . . . more evident in the sciences than in the arts subjects, and this consideration (among many others unconnected with student numbers) has conditioned the committee's approach to the determination of the block grant".

Table 1 Recommended Distribution of Money for different Subjects during 1972—77*

Medicine and Dentistry	102
Social and Business Studies	101
Architecture and Planning	101
Education	100
Arts	99
Veterinary Science	99
Mathematics	98
Agriculture and Forestry	97
Engineering and other Technologies	96
Physical and Biological Studies	95

* Percentage of present expenditure per student.

The UGC also makes the following suggestions to the universities.

- That computer sciences be strongly developed as well as statistics, operational research, and numerical analysis.

- That undergraduate computing courses be further encouraged.

- Electronic, electrical and production engineering and engineering design be encouraged. Also that broad-based research training and undergraduate courses in the technologies be favoured.

- Money allocated to engineering and physical sciences departments be more than the recommended average of 95 or 96, because these departments have many costly research programmes.

- The UGC would welcome the development of undergraduate courses with an education component combined with another subject such as mathematics or science.

SPACE

Pie in the Sky

BRITAIN and the United States have completed formal arrangements for the National Aeronautics and Space Administration to launch the Department of Trade and Industry's Earth satellites on a contract basis. The agreement is simply the formalization of an understanding reached in 1971 after Britain had decided to scrap Black Arrow (see *Nature*, **232**, 363 ; 1971).

The first satellite to be launched by NASA under the agreement will be X4, Britain's second technology satellite, which is scheduled for March 1974. The contract for the launch was signed on January 11 and the price DTI is to pay is about £1.25 million. The satellite is designed to prove a new 3-axis attitude control system, as well as a new solar array and a number of experimental sensors.

X4 will go up on a Scout launch vehicle, but DTI's next launch may be on a Delta rocket if the Geostationary Technology Satellite (GTS), on which Hawker Siddeley Dynamics and Marconi are currently working, goes ahead. It is at present scheduled for late 1976, but plans for the satellite may be changed if the plans laid by Mr Michael Heseltine, Minister for Aerospace and Shipping, for a European Space Agency come to fruition.

Advisory Board for the Research Councils

THE following are the members of the Advisory Board of the Research Councils which has replaced the Council for Scientific Policy.

Professor Sir Frederick Dainton (chairman), Dr Lee's Professor of Chemistry, University of Oxford ; Sir Kenneth Berrill, chairman, University Grants Committee ; Dr W. R. Boon, managing director, Plant Protection Ltd (ICI) ; Dr R. H. L. Cohen, chief scientist, Department of Health and Social Security ; Sir Brian Flowers, chairman, Science Research Council ; Dr J. A. B. Gray, secretary, Medical Research Council ; Professor F. H. Hahn, professor of economics, University of Cambridge ; Dr W. M. Henderson, secretary, Agricultural Research Council ; Professor Sir Alan Hodgkin, president of the Royal Society ; Dr P. E. Kent, exploration manager, British Petroleum Co. Ltd ; Mr D. J. Lyons, director general of research, Department of the Environment ; Dr I. Maddock, chief scientist, Department of Trade and Industry ; Professor R. C. O. Matthews, chairman, Social Science Research Council ; Dr A. W. Merrison, vice-chancellor, University of Bristol ; Professor W. S. Peart, professor of medicine, St Mary's Hospital Medical School, University of London ; Dr H. C. Pereira, chief scientist, Ministry of Agriculture, Fisheries and Food ; Dr O. Simpson, chief scientific officer, Cabinet Office ; and Professor F. H. Stewart, chairman, Natural Environment Research Council.

More Shuffling of the Pack

by our Washington Correspondent

SWEEPING changes in the federal science policy machinery are expected to be announced by President Nixon this week. At the beginning of the week, the final touches were being put to a reorganization plan which will abolish the Office of Science and Technology, the President's Science Advisory Committee and the position of Science Adviser to the President and give the director of the National Science Foundation responsibility for advising the White House on policies for civilian science and technology. The task of advising the President on policies for military research and development will be transferred from the OST to the National Security Council, the chairman of which is Dr Henry Kissinger.

The reorganization plan will give Dr Guyford Stever, director of the National Science Foundation, the dual responsibility of managing a federal agency and offering advice to the White House on general policy matters. But his advice will not go directly to the President but to the President's Economic Adviser, Dr George Shultz, who has recently been given the role of coordinating US economic policy (see *Nature*, **241**, 158; 1973). The effect will, therefore, be to shift responsibility for advising on science policy from the President's Science Adviser, who at least had direct access to the President, to the head of a small government agency who has access only to a presidential adviser.

As for the OST, its demise has been predicted since Dr Edward E. David, who was director of the office and Science Adviser to the President, left Washington in a surprise move earlier this month (see *Nature*, **241**, 82 ; 1973). Some of its staff are likely to be transferred to the National Security Council, others to the National Science Foundation, a few may go to the Office of Management and Budget, and the rest will be out of a job.

Sources close to the White House said this week that the initial idea will be for the National Science Foundation to be concerned chiefly with advice on civilian science policy, but advice on biomedical research policies will continue to come from the National Institutes of Health. There is some chance, however, that Dr Stever's role may eventually be broadened to include these fields as well.

The National Science Board, the policy-making body which helps direct the work of the National Science Foundation, is likely to take on some of the functions that were the responsibility of the President's Science Advisory Committee. But its advice will go first to Dr Stever, then to Dr Shultz, then to the President and it will not concern itself directly with military research and development. The National Science Board has published reports on an annual basis for the past few years on various aspects of science policy, graduate education and manpower planning for example, but they have had little effect on the shaping of national policies. Whether it will have more effect in future will depend in part on the effectiveness of Dr Stever.

The new role envisaged for the National Science Foundation will in fact give it the functions that were assigned to it when the foundation was set up by congressional charter in 1950. The National Science Foundation Act gave the NSF the responsibility for evaluating the programmes of other agencies in the science field. But when the launching of Sputnik sent shock waves through the federal government, it was felt that the director of the NSF would not be able to provide strong oversight over mission-oriented science agencies, and President Eisenhower established the post of Science Adviser to the President directly in the White House. And five years later, President Kennedy set up the Office of Science and Technology, and gave it the task of coordinating the activities of all the federal agencies concerned with science and technology.

One reason why the wheel has turned full circle is that since 1968 the National Science Foundation has broadened its activities in supporting applied research—an amendment to the National Science Foundation Act, sponsored by then Representative Emilio Q. Daddario and Senator Edward M. Kennedy, gave the foundation authority to support applied as well as basic research. It was felt that this broader role enabled the National Science Board and the director of the foundation to take a better view of the whole federal involvement in science and technology. One factor which was unclear at the beginning of the week, however, is how Dr Stever will be able to resolve a possible conflict of interest. On the one hand, he will be director of an agency which receives federal support and on the other he will be advising the White House on how it should be distributing funds to science agencies.

Clean Air Act

by our Washington Correspondent

RESIDENTS of Los Angeles were given a nasty shock last week. They were told by the federal government that if the city's smog-laden air is to be cleaned up enough to comply with the Clean Air Act, they will have to cut their use of automobiles by more than 80 per cent during the summer and equip their cars with pollution control devices costing between $200 and $400.

Those extreme measures were proposed last week by the Environmental Protection Agency which was under a court order to devise a scheme for meeting the primary air quality standards—which are designed to protect health—in Southern California by 1977. What the agency has proposed is a system of petrol rationing, beginning in 1975, which by 1977 would reduce petrol consumption in the Los Angeles basin by 82 per cent between May and October, when pollution is at its worst.

If the scheme is carried out, it will quickly bring the area to a grinding halt, for Southern California is virtually built around the automobile—there are 10 million people in the Los Angeles basin and 6 million cars, and because the city is such a sprawling metropolis it is almost impossible to get from one part to another without a car. It is also said that apart from its numerous drive-in banks, restaurants and cinemas, Los Angeles even boasts a drive-in funeral parlour.

A federal requirement which would probably wreck the economy and lifestyle of Southern California should be sufficient to provoke a mass revolt. But, although there has been some outspoken opposition to the plan, few people have taken it seriously. Even Mr William D. Ruckelshaus, Administrator of the Environmental Protection Agency, made it clear when he unveiled the plan that he was only offering such a drastic measure because he was ordered by a court to come up with a scheme which would definitely meet the standards. His scheme may be unworkable, but it would comply with the Clean Air Act.

The EPA's plan will be the subject of public hearings in Los Angeles in the next few months and, as Ruckelshaus pointed out last week, it will at least compel people to face the consequences of cleaning up Los Angeles air. In effect, the EPA has said to residents in Southern California that this is the cost of bringing air quality to a level at which it no longer presents a hazard to health, and the cost must now be weighed against the benefits.

If the costs are considered unacceptable, the most likely recourse would be to amend the Clean Air Act to give Southern California more time to comply. That would be the responsibility of Congress, and it would open the floodgates to special pleading from other cities having a tough time meeting the standards.

It can be argued, however, that the Los Angeles basin is a special case. For one thing, it is the unfortunate possessor of a sunny climate and for another it is flanked on three sides by mountains—two factors which combine to cause the infamous Los Angeles smog. What happens is that there are frequent temperature inversions over the basin in the summer, and the air hangs over the city, trapped in by the mountains. The six million cars in the basin continue pouring exhaust gases into the stagnant air, and in the presence of sunlight, hydrocarbons react with oxides of nitrogen to form the brown smog of photochemical oxidants which makes the surrounding mountains disappear in the afternoon.

The air quality standards imposed by the Clean Air Act would restrict the concentration of photochemical oxidants to 0.08 parts per million, but in 1970 that standard was exceeded in the Los Angeles area on more than 250 days. And the growth of the automobile population in the area—between 3 and 4 per cent a year—is continuing to exacerbate the problem.

In most areas in the United States, the air quality standards can be met by placing emission controls on stationary sources of pollution and by the stringent emission standards required for cars by 1975. But it soon became clear that in Los Angeles such measures would hardly make a dent in the air pollution problem and that some form of transportation controls would have to be imposed. The EPA reckons that by 1977, even with controls on stationary sources and automobile exhausts, some 691 tons of reactive hydrocarbons would be poured into the atmosphere each day; to achieve the national standard of 0.08 parts per million of photochemical oxidants, the agency calculates that hydrocarbon emissions must be reduced to 161 tons a day.

As for the petrol rationing proposal, the EPA has not spelled out how it should be implemented, but suggests either that motorists should be given coupons or that production should be rationed. In addition, catalytic converters must be fitted to the exhaust systems of all cars made since 1965, to convert carbon monoxide and hydrocarbons into carbon dioxide and water, devices must be attached to prevent the escape of fumes from the petrol tank and carburettor, and all cars and lorries in fleets of ten or more must be converted to run on low polluting fuels such as natural gas.

What happens next? It seems that two avenues are open if it is decided that the EPA's scheme would result in unacceptable social and economic dislocation. Either the EPA can propose a less drastic scheme, on the basis of submissions to the public hearing, which would only go part of the way towards meeting the standards, or Congress can amend the Clean Air Act to provide an exception for Southern California. Both options would, however, have serious implications for the future of the Act. In the meantime, the state of California, whose original plan for meeting the standards was rejected by the EPA, has until February 15 to draw up a revised plan of its own. Clearly, however, it will be no more successful in devising an acceptable plan than the EPA.

If the EPA decides to relax its scheme without waiting for Congress to amend the Clean Air Act it would break the law and be liable to a court action. In that case, its lawyers would probably argue that the act is unenforceable in the specific situation in Los Angeles, and if such a plea were successful, the agency could be given some leeway by the courts. The EPA would, however, be skating on thin legal ice. The other alternative—Congressional action to provide relief for Southern California—would probably be instigated by California's two senators, John Tunney and Alan Cranston. Both have denounced the EPA's plan, and Tunney has suggested that more attention should be paid to mass transportation as a means of reducing automobile traffic in Los Angeles. But so far neither has shown any indication of offering an amendment to the Clean Air Act.

Whichever alternative is adopted, Ruckelshaus can be certain that he will be assailed by representatives from other cities pleading for special treatment as well. Twenty-seven other areas in the United States must impose some type of transportation controls if they are to meet the standards imposed by the Clean Air Act, and although their controls would be minor in comparison to the Los Angeles plan, they could

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NUTRITION

What's in a Name?

by our Washington Correspondent

THE Food and Drug Administration has proposed sweeping changes in the labelling and promotion of food products in the United States. Described by Dr Charles C. Edwards, Commissioner of the FDA, as "the most significant change in food labelling since food labelling began", their purpose is chiefly to give consumers more extensive information about the nutritional value of the food they eat. The proposals have been greeted with mixed reactions from food manufacturers, some of whom have complained that they will increase the price of foods, and from consumer groups, some of which have suggested that the proposed regulations do not go far enough.

Companies which fortify their foods with nutrients, or which make advertising or labelling claims about nutritional value, will have to specify on the labels the number of calories and the quantity of protein, carbohydrates and fat in each serving. In addition, levels of vitamins and minerals must be specified in terms of the recommended daily allowance (RDA) rather than the minimum daily requirement. RDA levels have been established by the FDA largely on the basis of advice from the National Academy of Sciences. They are higher than the minimum daily requirement levels, and should be less misleading.

Aware of the fact that many companies now list ingredients in the most inconspicuous manner possible, the FDA is also proposing that nutritional labelling should be standardized and placed in a particular location on the package.

The agency has also proposed that all products marketed as dietary supplements must contain between 50 and 150 per cent of the RDA for certain specific vitamins and minerals. If they contain less than 50 per cent of the RDA for these vitamins and minerals, they must be classified as foods, or if they contain more than 150 per cent, they must be marketed as drugs and meet stiff tests of effectiveness.

The regulations have taken ten years to draw up, and manufacturers have been given until December 31, 1974, to comply. The most severely affected companies will be those which are attempting to cash in on the present "health food" fad in the United States by making false or exaggerated claims about the nutritional value of their foods. No longer will they be able to claim that natural vitamins are more effective than synthetic vitamins, or that inadequate or insufficient diet is caused by the soil in which a food is grown.

plead hardship with some conviction. They have until February 15 to come up with their plans.

But the Los Angeles smog is not Ruckelshaus's only worry in relation to the Clean Air Act. Acute shortages of low-sulphur fuels in the United States are likely to prevent some states from putting into effects their plans for meeting the sulphur oxides standards prescribed by the act, and the situation is likely to be exacerbated by the so-called energy crisis.

A study conducted by the Mitre Corporation for EPA has come to the conclusion that there will be insufficient quantities of low-sulphur fuels available, particularly in the Midwest, to allow all the plans to be put into effect, and it suggested that some states which have relatively pure air should be deregulated. The effect would be to increase sulphur dioxide pollution in those states, although it would not increase enough to exceed the primary air quality standards. Moreover, the "energy crisis", which has rapidly taken over from the "environmental crisis" as the chief topic of conversation in the United States, is likely to harm the environmentalist bandwagon in general and the Clean Air Act in particular.

Exceptionally cold weather earlier this month caused such a shortage of heating oil that schools and offices were closed all over the Midwest, and other areas were preparing for power breakdowns. President Nixon is due to outline the Administration's policies for coping with the energy crisis in a message to Congress in February or March, and it is widely expected that he will call for a greater reliance on coal for electricity generation—a move which would not help solve the problem of the shortage of low sulphur fuels.

But Ruckelshaus, for one, can be expected to fight hard to preserve the Clean Air Act from moves to weaken it. He has already refused to give automobile manufacturers extra time to develop emission control devices, in spite of a recommendation from the National Academy of Sciences, and his hard-nosed management of the EPA during his first two years in the job has won him wide respect from all sides. He said last week that he would like more flexibility in administering the provisions of the Clean Air Act, but that the act is "a great success". Just "because 5 per cent of it may not be working doesn't mean you ought to junk the whole act", he said.

CIGARETTES

Smoking and Health

from our Washington Correspondent

SINCE 1964 the US Public Health Service has published seven reports surveying the evidence linking cigarette smoking to disease and premature death. All have found that cigarette smoking is not only a major cause of lung cancer and chronic bronchitis, but that it is also associated with illness and death from chronic bronchopulmonary disease, cardiovascular disease and other illnesses. The latest in the series, published last week, is no exception. According to Dr Merlin K. DuVal, who resigned last month as Assistant Secretary for Health, it "confirms all these relationships", and it also has disquieting things to say about the effects of smoking on foetal development and mortality. The report also takes a look, for the first time, at brands of little cigars which are becoming popular in the United States. It concludes that if they are smoked in the same manner as cigarettes, they are likely to have the same effect on the health of the smoker.

As for the effects of smoking on pregnancy, the report points out that in 1970 one-third of American women of child-bearing age were cigarette smokers and it is estimated that the percentage of American women who smoke during pregnancy is "in the neighbourhood of 20 to 25 per cent". A large foetal population is therefore at potential, though preventable, risk.

The report comes to the following conclusions about the effects of smoking on the foetus:

- On the average, a woman who smokes during pregnancy runs nearly twice the risk of delivering an infant of low birth weight as that of a non-smoker, and there is strong evidence of a dose-response relationship.
- Recent studies suggest that "cigarette smoking is most strongly associated with a higher stillbirth rate among women who possess less favourable socio-economic surroundings or an unfavourable previous obstetrical history".
- There is a "strong, probably causal" association between cigarette smoking and higher late foetal and infant mortality.
- No conclusions can be drawn about any relationship between smoking during pregnancy and congenital malformation.
- Smoking does not seem to influence the sex ratio of newborn infants.

Short Notes

Institute of Medicine

THE Institute of Medicine, an associate institution of the National Academy of Sciences, announced last week that it has been given a grant of $300,000 by the Richard King Mellon Foundation in support of its general operations. The grant will be paid in three annual instalments, and it brings the total amount granted to the institute for the next three years to $1.5 million.

Reshuffle at NIH

TOP officials at the National Institutes of Health were shuffled around last week in a manner resembling a strange game of executive musical chairs. Dr John F. Sherman, Deputy NIH Director for the past four years, was promoted to Acting Director of NIH. Dr Robert Q. Marston, who was fired last month as NIH Director, was appointed Acting Director of an NIH institute, the National Institute of Neurological Diseases and Stroke (NINDS), and Dr Edward F. MacNichol, NINDS Director since 1968, left NIH partly of his own volition.

The moves suggest that Sherman will probably be given the full directorship of NIH, although there is still a possibility that President Nixon could appoint somebody else. But Marston's appointment is a temporary one, to ensure administrative continuity while a new NINDS director is chosen. Marston was informed last month that President Nixon had accepted his *pro forma* resignation as NIH Director, but no reasons have yet been publicly stated. MacNichol, on the other hand, resigned on his own initiative. It was revealed, in September 1971, that he had spent several months at Woods Hole while drawing government travel funds of $25 a day—a fact which led to a review by the General Accounting Office and by the NIH head office of government travel grants—but MacNichol retained his post without any change of status.

The reshuffle therefore puts Sherman in authority over his former boss and Marston in a dead end job.

US/USSR Cooperation

COOPERATION between the United States and the Soviet Union on environmental problems is continuing apace. This week, a joint working group met in Moscow to discuss wildlife conservation, and the Council on Environmental Quality, which is looking after the US end of the cooperative agreement, announced last week that fifteen other joint meetings have been arranged for 1973 on topics ranging from air and water pollution to earthquake prediction. Meanwhile, the chief cooperative agreement between the United States and the Soviet Union on science and technology is theoretical. The first meeting of the Joint Commission which was set up by the agreement has twice been put off, and Dr Edward David's departure from the Office of Science and Technology has left nobody officially in charge of the US end of the agreement.

NEWS AND VIEWS

Phytoagglutinins and Mammalian Sperm Penetration

In mammals, no less than in lower vertebrates and invertebrates, the means whereby the spermatozoon enters the egg to effect fertilization has long been a puzzle. First attachment occurs as the result of an "effective" collision by the spermatozoon, and this seems to be a necessary preliminary to penetration of the investment. The high degree of specificity in the process of attachment constitutes a bar to hybrid fertilization. At the same time, by no means every spermatozoon that becomes attached succeeds with penetration, for this too is generally reserved for spermatozoa of the same, or a closely related, species. Furthermore, in mammals particularly, the egg investment (zona pellucida) reacts so as to become more resistant after the entry of the first spermatozoon, and thus the frequency of multiple or polyspermic fertilization is minimized. Polyspermy is a normal feature of fertilization in some organisms, such as birds and reptiles, but in mammals it leads inevitably to maldevelopment and, nearly always, death of the growing embryo.

Clearly the properties of the zona pellucida are highly important for the initiation of normal development, and many attempts have been made to elucidate the nature of the zona pellucida and the mechanisms of sperm attachment and penetration. Early work showed the zona pellucida to be a neutral or weakly acidic mucoprotein which could be crudely characterized by its staining properties, and its solubility following treatment with enzymes and other agents. After sperm penetration, changes were recorded which seemed to have been associated with the zona reaction. But none of these observations helped materially towards a satisfactory understanding.

On page 256 of this issue of *Nature*, Oikawa, Yanagimachi and Nicolson describe experiments with plant agglutinins, and their report could well signal a new and fascinating phase of research on sperm-egg interactions. In essence, these authors find that treating hamster eggs with wheat germ agglutinin not only reduces sperm attachment to the zona pellucida but prevents their penetration of this structure, and inhibits its dissolution by several otherwise highly effective enzymes. Treatment increases the light-scattering property of the outer surface of the zona pellucida, suggesting a change in molecular organization there. These effects are prevented if the specific substrate, N-acetyl-D-glucosamine, is present in sufficient concentration, implying the presence on the surface of the zona pellucida of oligosaccharides containing terminal residues of this kind.

Oikawa *et al.* propose that the phytoagglutinin forms cross-links between the oligosaccharide chains of adjacent glycoprotein molecules, and thus prevents dissolution of the coat by experimentally applied enzymes. Cross-links would also render attachment sites unavailable and would tend to counter the action of the postulated "zona lysin" which is held to function by digesting a path for the spermatozoon through the zona pellucida. Certain other phytoagglutinins have a similar blocking action ; this was found to be true particularly for the *Ricinus communis* agglutinin, which attaches to β-D-galactose-like residues, and the *Dolichos biflorus* agglutinin, which attaches to N-acetyl-D-galactosamine-like residues, but rather less so for concanavalin A, which attaches to α-D-mannose-like residues. One can therefore infer that a variety of saccharide residues in the surface of the zona pellucida are critically involved in the process of fertilization.

The identity of the saccharide residues on the zona pellucida could well determine the species specificity of sperm-egg attachment. They would constitute "recognition" sites such as seem likely to be involved in cell aggregation during embryonic development or following artificial disaggregation in culture. A basic difference would, of course, be that the recognition sites exist on plasma membranes, from which the zona pellucida differs in several particulars. Nevertheless there are some important similarities. Just as the plasma membranes of cells that are undergoing transformation exhibit changes in surface properties, the sperm permeability of the zona pellucida is capable of alteration with the occurrence of the zona reaction and with the ageing of the egg.

A homology between attachment sites of phytoagglutinins and antibodies seems undoubted, and the observations of Oikawa and his colleagues are complementary to those of Shivers, Dudkiewicz, Franklin and Fussell (whose unpublished paper they cite) who blocked the fertilization of hamster eggs by prior treatment with a rabbit antibody raised against hamster ovary. The effect was shown to be attributable to antibodies against the zona pellucida, and the block was associated with a change in the optical properties of the outer layer of this coat. As with the wheat germ agglutinin, treatment with antibody protected the zona pellucida from dissolution by protease. Whether the antibody would block attachment of the phytoagglutinin, and vice versa, has yet to be determined. *A priori*, such a result might be anticipated.

There are good signs that with their homogeneity and high specificity the phytoagglutinins could prove invaluable new tools for the investigation of gamete structure and function in mammals.—C. R. A.

Fixes on Radio Sources

Optical identification becomes possible for some types of radio object as soon as radio source catalogues have errors of position better than 1 arc s r.m.s. in both right ascension and declination. For the identification to be certain, an optical accuracy of better than 1 arc s in each coordinate is required, and, further, if the object is condensed and nearly stellar then it must be either a blue object or a galaxy fainter than 19 magnitude. On page 261 of this issue of *Nature*, Gent *et al.* report a revised identification of eleven radio sources, three of which have now been identified with stellar objects that are neutral in colour. The certainty of identification has been made possible by the increased accuracy to 0.5 arc s r.m.s. in each coordinate using measures obtained from the interferometer at the Royal Radar Establishment. What will a spectroscopic investigation of these sources reveal about their nature? Will they turn out to be quasars with high redshifts or an entirely new class of object?

The earliest attempt to obtain accurate optical positions of radio sources was made in 1963 by R. Griffin, and it was several years before the same degree of accuracy was attained again. He used plates from the 48-inch Palomar Schmidt and an average of ten comparison stars whose positions were well determined in each of forty-two fields. The standard stars were chosen from the best catalogues then available, namely the Yale Zone catalogue and the AGK2, and the effects of proper motion were ignored. To achieve the desired accuracy of less than 0.5 arc s r.m.s. in the optical positions of star-like objects fainter than 18 magnitude there are three chief requirements: first, an adequate plate scale of, say, 60 arc s mm^{-1} or better; second, good images of the reference stars, which will probably be brighter than 12 magnitude, and the quasar, which may be fainter than 18 magnitude; and, third, a wide field of at least one degree to yield a good sample of comparison stars.

Unfortunately, there are only a few instruments, such as the 48-inch Schmidt, which have these qualities. This situation is likely to be somewhat alleviated in the near future, because two new large Schmidt telescopes (one at the European Southern Observatory in Chile and one at Siding Spring in Australia) should become operational later this year (see *Nature*, **239**, 489; 1972). But even with these new instruments the total load will be too great for the available wide-field instruments. The Isaac Newton Telescope, for example, has all the desired qualities at the prime focus except that the field of three-quarters of a degree is often too small to find enough comparison stars from the AGK3. It becomes necessary to use another telescope with a larger field to set up a secondary sequence of standards. There will clearly be difficulties encountered with unknown errors caused by the large ranges in magnitude and colour of the objects measured.

Nowadays it is customary to use lists prepared by a computer of stars within one degree of the quasar, taken from the AGK3 or the Smithsonian Astrophysical Observatory catalogue, and to apply proper motions to bring the star places to the epoch of the photographic plate. The reduction of the star measures made on digitized measuring machines is also computerized, using well-known equations for the plate reduction and the method of least squares.

The rapid progress of radio interferometry, notably by Sir Martin Ryle and the group at Cambridge, has increased the accuracy of radio positions until they equal or better their optical counterparts. One important question arises—does the optical and radio emission of small-diameter sources come from the same position in the sky? The affirmative answer is implicit in the work of Sandage, Kristian and Wade (*Astrophys. J.*, **162**, 399; 1970) although a counter example may have been found by Gent *et al.*

The increased accuracy of the radio interferometers has introduced a new aspect into the derivation of a fundamental system for star positions which was not envisaged a few years ago. Optical astronomers have been interested for a long time in using the galaxies as a fundamental reference frame without realizing that one day they could use the small faint point sources of quasars. In fact radio interferometers give absolute positions and it is imperative to provide a frame of reference for calibrating radio against optical positions. The most important step in this direction was made by Murray, Tucker and Clements (*Roy. Obs. Bull.*, No. 162, 215; 1971) when they attempted to refer their positions directly to the FK4 system by using observations of comparison stars made with the transit circle. As Fricke has pointed out, technically there is no longer any obstacle to the extension of the fundamental system from the brightest stars to faint quasistellar objects.—From a Correspondent.

Age and Cancer Incidence

THE factor correlated most strongly with the rate of cancer incidence in humans is undoubtedly age; the probability that a man will develop a cancer in the next five years is 1 in 14 if he is 65, but only 1 in 700 if he is 25 (figures for Birmingham (UK), from *Cancer Incidence in Five Continents,* UICC, 1970). This represents a relative risk of about 50 to 1, and similar orders are found in many different animal species if the total rates of cancer incidence in late and early adult life are compared. In countries with adequate cancer registries, total cancer incidence can be separated into incidence rates for each organ of the body, and most of these separate rates increase between the ages of 25 and 65 approximately as the fourth or fifth power of age.

The process of transforming normal tissue into a pathological cancer can be shown to take place in several distinct "stages", each with its own causes. Many animal cancers, for example, are evoked only when a dose of an "initiator" is followed, perhaps months later, by a dose of a "promoter"; but not if these stimuli are given in the wrong order. Moreover, the incidence of human lung cancer is higher in ex-smokers than in non-smokers of the same age long after termination of smoking, which suggests that smoking acts on some earlier stage rather than the final stage of carcinogenesis.

If the kinetic rate-constants of the various stages of cancer are approximately independent of age, then in a five-stage system the rate at which cancers would arise in a large population of animals would be proportional to the fourth power of age. This means that the dependence of human and animal site-specific cancer rates on a power of age can be explained simply by assuming that a number of stages are involved and that no strong associations exist between age and the kinetic rate-constants of the various stages. Although it has been possible for decades to generate and study cancers in experimental animals, there is still little understanding of what these different stages may be.

Some stages may be specific mutations in cells in the target tissue, the occurrence of ageing processes in these cells, or they may be systemic, affecting equally all the organs in the body; if immunological elimination of pre-cancerous lesions is normal, for instance, then one or more of the stages may involve damage to this mechanism. There are two techniques which may prove capable of distinguishing between systemic stages and local stages, and of separating the effects of ageing from the mere accumulation of cells in the body which have already passed through the first stage(s). The effects of the same carcinogen given at different ages can be studied; if a carcinogen can be found which elicits exactly the same response at all ages, then it will be possible to conclude that immunological changes and changes within the tissue caused by ageing are irrelevant. (Experiments to find such a carcinogen are now nearing completion.)

The other experimental technique is the transplantation of tissue from one animal to another, followed by chemical induction of cancer in the transplanted tissue. This has already been used to show that tissue from cancer-resistant or cancer-susceptible animals remains resistant or susceptible depending on the resistance of the host animal (Cowen, *Brit. J. Cancer*, **13**, 228 ; 1959). These experiments, however, related only to benign tumours and were not carried out in sufficient detail to exclude completely a relationship between the host and the eventual outcome; for this, it would have been necessary to have studied the fates of similar transplants in a variety of different animals. On page 280 of this issue of *Nature*, Ebbesen reports an experiment in which different transplants are given to similar hosts. He demonstrates that, unless an artefact has been produced in which sebaceous gland differences alter the effective dose of 7,12-dimethylbenz[α]-anthracene (DMBA), skin transplanted from old mice is more susceptible to carcinogenesis by DMBA than is skin transplanted from genetically similar young mice. This situation suggests that some at least of the increase in cancer incidence with old age is attributable to local changes in the target tissue.

Unfortunately, the effect that Ebbesen detects is much less marked than the expected effect of age on total cancer incidence. Moreover, the cancers evoked are benign rather than malignant, and the complementary experiments in which similar tissues are tested after transplantation into mice of different ages and in which DMBA is applied to untransplanted mice of different ages have not been carried out. But the technique of transplanting tissues of various ages into hosts of various ages is obviously very promising for determining the relevance (if any) of immunological or any other systemic changes in carcinogenesis.—R. P.

Electrons, Muons and QED

THE quantum theory of the electromagnetic field, quantum electrodynamics, now correctly predicts all relevant experimental phenomena over distances ranging from 2×10^{-15} cm out to 80 Earth radii, a span of more than 10^{20}, one of the greatest success stories in physics. The simplest possible system to study is the free electron, and for this the quantum fluctuations of the electromagnetic field close to the particle imply an apparent increase in its magnetic moment beyond the value of one Bohr magneton implied by the unmodified Dirac theory. So the gyromagnetic ratio (of magnetic moment to spin angular momentum in atomic units) is increased from 2 by the factor of 1.0011596527(24), the error on the last two digits being indicated in parentheses. This theoretical expression is known to 5 parts in 10^{10} from new calculations (Kinoshita and Critanovic, *Phys. Rev. Lett.*, **29**, 1534; 1972; Calmet and Peterman, to be published). To achieve such precision the theoretician must take into account a multitude of rare fluctuations, which create ephemerally around the electron a variable swarm of accompanying photons and electron-positron pairs. Fortunately they can all be specified in terms of the Feynman rules, but nevertheless in several laboratories many man-years have been devoted to the problem.

The predicted value depends, of course, on the strength of the electron's coupling to the electromagnetic field as specified by the value of the fine structure constant α, which is known to 1.9 parts per million. This contributes an uncertainty of 22 parts in 10^{10} to the gyromagnetic ratio g, and is the chief ingredient of the error already quoted.

Experimentally the magnetic moment of the electron can be measured by studying its precession at rest in a magnetic field, but as the Bohr magneton itself is not known to much better than 1 part per million this would not lead to an accurate value for the g factor. It is possible, however, to measure directly the value of $(g-2)$; that is, experiments can be arranged which are directly sensitive only to the small correction occasioned by the quantum fluctuations. If a polarized electron is projected into a magnetic field so that it describes many almost circular orbits, then for $g=2$ it can be shown that the angle between its spin and its momentum must remain rigorously constant. So even after many turns the direction of polarization (relative to the direction of motion) would be the same. As g is in fact greater than 2 the polarization slowly changes: by measuring the spin-momentum angle as a function of time the value of $(g-2)$ can be determined directly.

In a twenty-year programme Crane and his colleagues at Ann Arbor, Michigan, have gradually refined the measurement of the electron "gyromagnetic anomaly", the current result being $g=2\times1.0011596567(35)$, in excellent agreement with theory (Wesley and Rich, *Phys. Rev.*, **A4**, 134; 1971; Granger and Ford, *Phys. Rev. Lett.*, **28**, 1479; 1972). The anomaly is checked to ±4 parts per million, thus giving a remarkable confirmation of the theory and the procedures of quantum electrodynamics. Alternatively, if one believes the theory, the result can be interpreted as an independent measurement of α to an accuracy of 3 parts per million, adding significantly to existing knowledge based on other methods. If the accuracy could be further improved the electron gyromagnetic anomaly could give the most accurate, and certainly the cleanest, measurement of the fine structure constant. Nothing prevents this in principle, but who will undertake the painstaking effort involved?

An even better test of the theory is offered by the muon, which behaves exactly like an electron although it is 206.768 times heavier. It also has a gyromagnetic ratio of 2 plus a small correction: but because of the higher mass the quantum fluctuations involve energies 200 times higher and, in particular, evanescent electron pairs are created more frequently. Indeed, pairs of pions and other strongly interacting particles are present, often to a sufficient extent to contribute to the g factor. For the muon, also, a $(g-2)$ experiment is possible and has been carried out at CERN (Bailey *et al.*, *Nuovo Cimento*, **9A**, 369; 1972); this gives $g=2\times1.00116616(31)$, compared with the theoretical value (Lautrup, Peterman and de Rafael, *Phys. Rep.*, **3C**, 193; 1972) of $g=2\times1.00116588$. The agreement to 240 ± 270 parts per million in the anomaly is less accurate than for the electron, but because of the higher mass of the muon it has provided one of the best tests of quantum electrodynamics at small distances (high energy), where departures from the theory (if any) are most likely to show up. This practically guarantees that the theory for the electron is good enough for a precise measurement of α to be trusted.

A new muon ($g-2$) apparatus is now being prepared at CERN. It involves a ring magnet 14 m in diameter in which the muon will turn thousands of times, and should give g to about 1 part in 10^8. At this level quantum fluctuations involving heavy particles will be seen clearly, and may well lead to some surprises. Nobody can be sure that the effect of strong interactions between these particles has been estimated correctly, and of course undiscovered particles have not been taken into account, although obviously the muon itself may be aware of them. In particular somewhere, some day, one expects to find out why the muon is so heavy. If this can be attributed to a private particle coupled only to the muon, it could show up as a correction to the g factor. —From a Correspondent.

ENERGETICS

What Price a Weasel?

from a Correspondent

LONG, thin mammals like weasels need more energy to run than do compact mammals like rats, according to James H. Brown and Robert C. Lasiewski (*Ecology*, **53**, 939; 1972). By comparing metabolic rates of weasels (*Mustela frenata*) with wood rats of the same weight (*Neotoma* spp.) at various temperatures, they found a 50–100 per cent increase in the metabolism of weasels. Three factors seem to govern this difference—the surface area of weasels is greater in proportion to the mass of the body than it is in the wood rat; their fur is less than half as long as that of the wood rat and has a correspondingly lower insulative quality, and, third, weasels are unable to attain a spherical or near spherical resting posture. Combined, these factors make the cost of thermoregulation rather high for the weasel as so much energy is dissipated as heat.

The high cost of thermoregulation, however, must have been offset during evolution by the advantages of a long thin body able to penetrate small cracks and burrows in pursuit of prey. The fact that many species of weasels and their relatives inhabit northern temperate, sub-arctic and even arctic regions is proof of their ecological fitness. Brown and Lasiewski suggest that energetic efficiency has been sacrificed for enhanced predatory ability and, presumably, efficiency. A correspondingly greater amount of predation is necessary to support the energetically inefficient body shape. The application of Bergmann's rule, that animals evolve more compact shapes in cold climates to protect against undue heat loss, does not seem therefore to apply to weasels.

Brown and Lasiewski hit on a most interesting ecological point when they discuss sexual dimorphism of weasels. Males are significantly larger than females and may weigh up to twice as much. Ecologically this means that male and female weasels occupy virtually different feeding niches. Small fissures and burrows and the prey within them are exploited by the females, and larger crevices and the like are exploited by the male. Thus intersexual liaison benefits the species in that a territory is more fully exploited, as if by two species. Intrasexual competition, necessary for the maintenance of spacing patterns and population stability, is enhanced because of the weasels' increased energy requirement. The spread into a second niche through the agency of sexual dimorphism is not unique in the animal kingdom; in some deep sea fishes it is normal for the male to be parasitic upon the female. (Not only does this make the union of male with female easier, but it has important economic advantages in energetically impoverished environments.) The impact of *M. frenata* on the environment is essentially like that of two separate species.

Among the Mustelidae only those species with an elongate body form show marked sexual dimorphism. Obviously the elongate form and the sexual dimorphism evolved together, and now are totally dependent upon one another. It seems that only by evolving into a secondary, sex specific niche by means of sexual dimorphism, can sufficient energy be harvested to allow the energetically inefficient body shape to function as a more efficient predatory machine. This has the effect of increasing the rate of energy flow in the environment—a useful feature in regions of intrinsically slow turnover—and of increasing the number of filled ecological niches without requiring the introduction of additional species. Bergmann's rule, if it applied in this instance, would be prejudicial to the development of the community, and to the expression of maximum ecological vitality.

TRANSFER RNA

Through Fields of Clover

from our Molecular Biology Correspondent

WHETHER it is a good idea for physical chemists to seek to bend the bow of the crystallographers by the pursuit of structural information about biological molecules is no doubt a matter of opinion. It is safe to say, however, that protein models based on ultraviolet difference spectra, optical rotation and the like have not proved the most enduring monuments of modern science. In the RNA field the prospects of extracting relatively hard, if modest, information, such as the degree and composition of base pairing, have seemed altogether more propitious, and much effort, more some might feel than the objectives justify, has gone into the development of methods to do just this, and to apply them to species of known sequence, particularly the tRNAs. The answers have in general been compatible with the pairing schemes imposed by the celebrated cloverleaf structure, and

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Correlating Genetic and Translational Maps

IN *Nature New Biology* next Wednesday (January 31) Celis, Smith and Brenner report a set of those experiments in which molecular geneticists display their sophistication. Celis *et al.* have correlated the translational map and the genetic map of gene 23 of phage T4 (this phage has long been one of the happiest hunting grounds of molecular geneticists) and they find that for at least 40 per cent of this gene 0.012 recombination units of the genetic map correspond to one amino-acid residue in the gene 23 protein.

Gene 23 of phage T4 specifies a major polypeptide of the head of this phage. Furthermore, it has been shown that the polypeptide in the phage arises from the primary product of translation of gene 23 messenger from which an N-terminal fragment is cleaved. To compare genetic and translational maps of gene 23, Celis *et al.* measured the molecular weights and characterized by fingerprinting the fragments of gene 23 precursor protein specified by a set of amber mutants which had previously been genetically mapped. A plot of the molecular weights of the fragments of polypeptide against the recombination distances between these amber mutants yields a straight line, the slope of which is 0.012 recombination units per 100 daltons of polypeptide, in other words per amino-acid. In spite of one anomaly—the polypeptide specified by a mutant E161 is about a third smaller than predicted—Celis *et al.* believe they may have hit on a constant physical unit of recombination. Further studies of other genes should decide whether or not this is the case.

this is also the case with the latest, and undeniably most elegant, and very likely most precise approach yet, which involves the use of high-resolution proton magnetic resonance in water solution. The results, as readers at least of the *New York Times* will know, will all too soon be subject to the most searching of tests, for the heavy tread of the crystallographers is already shaking the tRNA field.

What Wong, Kearns, Reid and Shulman (*J. Mol. Biol.*, **72**, 725; 1972) have done is to look at the resonances from the exchangeable protons of yeast phenylalanine tRNA. For this purpose it is necessary to work in water, for in deuterium oxide these protons exchange out and their signals vanish, so that, as Wong *et al.* point out, the best structural information is thrown away. The difficulties of operating near an immense solvent signal must be considerable, but the interesting regions are far enough downfield to make the operation possible. Wong *et al.* divide their spectra, done at 220 MHz on 5 per cent solutions of RNA into three regions. In the first, which extends from −6 to −9 p.p.m., one observes non-exchangeable base protons, and the exchangeable protons of amino-groups in both paired and unpaired bases. In D_2O only the first group remains, and their contribution can thus be determined and subtracted from the spectrum in water. There are two broad peaks, one centred at about −8 p.p.m., the other nearer to −6.5 p.p.m., and on the grounds of their relative positions, and the emergence of the second peak only at *p*Hs appreciably below neutrality, where exchange with water is not too rapid, they are assigned respectively to paired and unpaired bases. The total numbers of protons contributing to the intensity of these two peaks are 67 and 45 per molecule, whereas that of the unexchangeable protons is 89 ± 4, which agrees with the count of 89 from the base composition.

The least equivocal results on the extent of base pairing come, however, from a set of resonances lying between about −11 and −15 p.p.m. which on the grounds of earlier work on model systems can be assigned to internally hydrogen-bonded ring NH protons, each base pair contributing one such (because one ring NH only, in U or G, is implicated in each Watson-Crick pair). The A·U and G·C contributions are separable, especially in one spectrum obtained with a new 300 MHz instrument, which resolves nine peaks in this region, and seven A·U and eleven G·C pairs are deduced to be present. The cloverleaf scheme gives eight and twelve, as well as one putative G·U pair, so that this model, so far as it goes, is upheld by the results.

The figure of twenty base pairs determines the interpretation of the intensities of the exchangeable amino-proton peaks: each amino-group involved in base pairing must contribute both of its protons to the slowly exchanging category. With two amino-groups per G·C pair and one per A·U, the total comes to sixty-four, which agrees with the experimental value of sixty-seven. This behaviour is also required by the tritium exchange results of Englander and his colleagues, and this strongly reinforces the interpretation. There is also a small group of resonances in a third region (−9 to −11 p.p.m.), the intensity amounting to 4 or 5 protons, which may perhaps arise from features of tertiary folding.

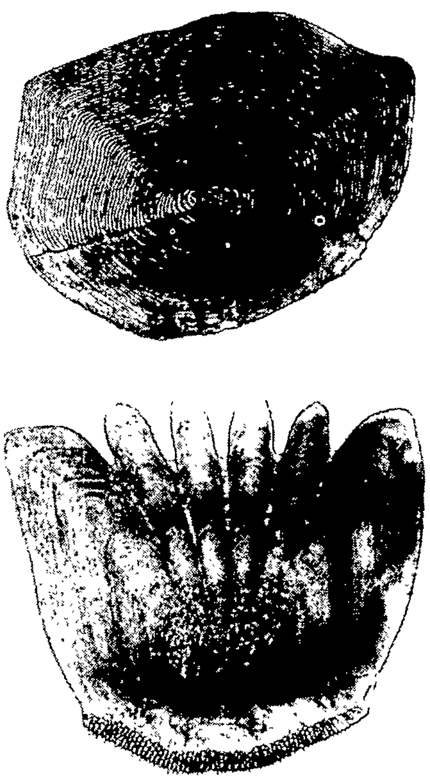
In an accompanying article (*ibid.*, 741) the same authors give the results of a similar study of the ribosomal 5S species, and come up with twenty-one base pairs in the absence of magnesium, and twenty-eight in the presumed "native" state, when magnesium is present. Some 85 per cent of the base pairs are found to be G·C. This, if taken at face value, is enough to rule out most of the models of 5S RNA that have been proposed. Wong *et al.* infer from the rather low degree of pairing that the structure is rather open, and support this view by demonstrating a higher susceptibility to T_1 ribonuclease than that of tRNA. In this connexion a salutary note of caution comes from Mirzabekov and Griffin (*ibid.*, 633), who have used T_1 digestion and nucleotide mapping to look for the labile points in the 5S RNA sequence, which are presumed to be in single stranded loops. Taking care to maintain the magnesium-dependent native conformation throughout, they find that one scission occurs between residues 61 and 62. This evidently allows the excision of residues 57 to 61, which are missing in one of the fragments. Two further regions of attack are between residues 16 and 17, and 18 and 19 at the 5′ end of the chain, and between 102 and 103 near the 3′ end (the total length being 120 nucleotides). The corresponding placement of loops seems again to rule out some feasible pairing schemes. What is most striking, however, is that the results differ from those of Jordan, who found, in equally definitive terms, a break between residues 41 and 42. This lends substance to the notion that the molecule may enter a number of energetically almost degenerate structures, the stability zones of which are not easily defined.

FRESHWATER FISHES

Keys to British Forms

from a Correspondent

THE basic problem facing most biologists at some time or another is the correct identification of the forms with which they are concerned. Those working on aquatic animals in the British Isles have been helped in the past by the scientific publications of the Freshwater Biological Association. The most recent in the series is *A Key to the Freshwater Fishes of the British Isles with Notes on their Distribution and Ecology*, by Peter S. Maitland (*Sci. Publ.*, No. 27, 139 pp.; 1972). In a sense this publication breaks new ground, for it deals with a vertebrate group which is well known, for which the literature is easily available and in which the animals are relatively easily identified. Moreover, several recent books on the market cover the same ground. The publication is, however, more than a plain key to British freshwater fishes. It contains, besides the chief keys to families and species, preliminary keys to fish eggs, larvae, and scales. Furthermore, it includes maps of the distribution of the fifty-five freshwater or euryhaline species found in the British Isles.



Typical scales from two contrasting British species of freshwater fish: above, cycloid type from the whitefish, *Coregonus lavaretus*; below, ctenoid type from the perch, *Perca fluviatilis* (plate taken from P. S. Maitland's new key).

These distribution maps bulk large at one per page in a publication of 139 pages. Nevertheless they provide valuable information in that they represent the results of a national scheme to collect data on the distribution of freshwater fishes. In 1969 Maitland (*J. Fish Biol.*, **1**, 45) outlined this scheme which was commenced a year or two earlier, and was later prosecuted by the Biological Records Centre of the Nature Conservancy. It seems most remarkable that this is the first systematic attempt to map the distribution of freshwater fishes in the British Isles. Earlier statements of their distribution were apparently generalizations, based on reports in literature or museum collections, of presence or absence in river systems. Maitland's work on the mapping of observed occurrences is therefore a welcome addition to basic data.

Records of occurrence are shown by the standard 10 km square grid used by the Biological Records Centre. Like all distribution maps, they are open to the comment always made of such projects—that they show the distribution of recording observers rather than the animals concerned. Although this is true to some extent, it is equally true that this first printing should act as a spur to laggardly recorders, and generate a need for updating and reprinting soon. One hopes that future editions of the maps will be available at a more realistic price than the £1.20 at present charged for the whole publication.

The identification keys are presented in the classical manner with couplets which use several, chiefly meristic, characters at each step. This results in the usual cumbersome arrangement in which no short cuts are permissible, and one mistake can lead to disaster; the student simply has to plough through all the appropriate couplets with the thought that there must be an easier way to identify a fish than counting scales, fin rays, myomenes, gill rakers and so forth. To take an example, to identify a flatfish from a British river, one needs to work through five couplets (out of twenty in the family key) to get to the family (Pleuronectidae) and a page reference, on which one discovers that there is only one species anyway—the flounder.

The example begs the question, why in a key which is presumed to be used in the field or by the beginner in fish taxonomy is it necessary to follow slavishly a systematic order, and to overload each couplet with detail? The flounder, being the only flatfish, could have been dismissed in a single line on the first page to the great benefit of the user and a considerable economy of paper and effort.

The practical result of such a classical method and prolixity will be despair in most cases, and the user forced to look for the "best fit" illustration. Keys intended for use in identification (as opposed to those concocted to show systematic positions, or the ingenuity of the compiler) should be simple and unambiguous, using characters which are, if not trenchant, then easy to assess. The only justification that can be offered for the present style is that a worker totally unfamiliar with the subject could use the key, but even the simplest student is likely to wonder at the choice offered in several couplets, as "Less than 13 rays in the anal fin . . ." *versus* "More than 11 rays in the anal fin . . .". There must be easier ways of identifying fish than this.

TRANSFORMATION

Genomic Parameters

from our Cell Biology Correspondent

ESTIMATES of the number of genomic equivalents of simian virus 40 DNA in cultured cells transformed by SV40 are markedly dependent upon the methods used to measure the amount of SV40 DNA in a known amount of cellular DNA. Westphal and Dulbecco, who developed a method for transcribing *in vitro* with *Escherichia coli* RNA polymerase SV40 DNA and then hybridized this labelled virus-specific RNA to transformed and untransformed cell DNA stuck to nitrocellulose filters, have estimated that cells of a particular line of SV3T3 transformants contained forty-four genomic equivalents of SV40 DNA. But when Gelb *et al.* estimated this parameter from measurements of the rate of reannealing of SV40 DNA in the presence of DNA from these SV3T3 cells and in the presence of untransformed 3T3 cells they came up with the value of 1.42 SV40 genomes per cell. Even allowing for the different values assumed by these groups for the weight of the 3T3 cell genome there remains a twenty-fold discrepancy.

It is nowadays generally accepted that the estimate of Gelb *et al.* is the more accurate, not least because, as Haas, Vogt and Dulbecco showed recently, DNA hybridized to RNA tends to come free from nitrocellulose filters, and, no doubt for the same reasons, Pettersson and Sambrook's estimate (*J. Mol. Biol.*, **73**, 125; 1973) that rat cells transformed by adenovirus 2 contain about one genomic equivalent of adenovirus 2 DNA per diploid amount of cell DNA is closer to reality than the estimates of fourteen to thirty-seven genomic equivalents of adenovirus 2 DNA per cell genome reported in 1970 by Green and his colleagues, who used the RNA/DNA hybridization technique. The transformed rat cells used by Pettersson and Sambrook were separate stocks, originally derived from the same transformant grown from many cell generations in different laboratories. Clearly the amount of adenovirus DNA in such cells is stable. Furthermore, because the transformed rat cells are aneuploid it is currently difficult to calculate just how many viral genomes there are in each transformed cell genome as opposed to per diploid amount of cell DNA, but the number must be very small.

Like adenovirus 2, adenovirus 12 transforms rodent cells, and according

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Taxonomy of RD114 Virus Particles

RD114 VIRUS is a C-type RNA virus liberated from a line of human tumour cells which was passaged in kittens. Because of the history of these human cells which liberate RD114 virus two possible origins of the virus have to be considered; it might be a feline virus picked up during the passage in kittens or it might be a human virus, related to the RNA tumour viruses of lower mammals, the replication of which was induced when the human cells were passaged in kittens. A variety of serological tests have shown that RD114 virus particles are not antigenically related to known feline C-type viruses, and in *Nature New Biology* next Wednesday (January 31) Huebner's group (Long *et al.*) report experiments which they believe "add to the indication that RD114 is most probably a human virus".

Long *et al.* inoculated partially purified RD114 virus particles into guinea-pigs and obtained from these immunized animals antisera which strongly inhibit the reverse transcriptase activity present in RD114 virions. They then assayed these antisera for their ability to inhibit the reverse transcriptase activities present in primate, feline, murine, avian and viper C-type RNA viruses. It has, of course, been shown repeatedly that the reverse transcriptases present in these different groups of viruses are antigenically distinct and that transcriptase inhibition tests using antivirus antisera indicate taxonomic relationships between these viruses.

Long *et al.* find that antisera to RD114 virions reproducibly and completely inhibit the reverse transcriptase in this virus and also inhibit to a significant extent the transcriptase activities in two primate C-type viruses. The anti-RD114 antisera do not, however, reproducibly inhibit the enzymes in feline, murine, avian and viper viruses. Clearly this result is compatible with the idea that RD114 is a human C-type virus, but it is surprising that Long *et al.* did not carry out the reciprocal tests, challenging RD114 particles with antisera against the two primate viruses; these tests should be done, for they may clinch the case.

to Champe, Strohl and Schlesinger (*Virology*, **50**, 482; 1972) tumour cells induced in hamsters by injections of adenovirus 12 contain a factor, resistant to digestion by nucleases but sensitive to pronase, that reduces by up to 99 per cent the yield of adenovirus 12 made in permissive cells infected by this virus. Champe *et al.* claim that this inhibitory factor decreases the rate of replication of adenovirus 12 in permissive human embryonic kidney cells as well as the final yield of virus from each cell and that it does not inactivate purified infectious viruses. This fact, and the observation that the factor does not inhibit T antigen synthesis in infected cells, leads them to conclude that the factor is more likely to inhibit some late events in adenovirus 12 replication than the adsorption, penetration and uncoating of the virus. The factor is virus specific and therefore not likely to be an interferon, but so far Champe *et al.* have no real idea as to its target.

Reznikoff, Tegtmeyer, Dohan and Enders (*Proc. Soc. Exp. Biol. Med.*, **141**, 740; 1972) have addressed themselves to a superficially at least not dissimilar problem, namely the identification of the resistance of certain AGMK cells to SV40. Most AGMK cells are fully permissive for SV40 and are killed by the virus as it replicates, but some AGMK cells become chronically infected rather than lytically infected and may even be transformed by SV40. Reznikoff *et al.* have investigated the effects of SV40 specific antiserum on such chronically infected AGMK cells. In the presence of this antiserum clones of chronically infected cells can be cured of all detectable traces of SV40 virus and its antigens, and at least one cured clone of cells cannot be infected by SV40 virions but can be infected and killed by naked SV40 DNA.

One simple interpretation of these data is that part of the resistance of these cells to SV40 stems from some block before the uncoating of the viral DNA, but there is almost certainly more to the story than that, not least because an absolute block to virus penetration and uncoating would obviously preclude the emergence of SV40 transformed AGMK cells.

SOLID STATE

More on Ferrofluids

THE properties of ferrofluids—liquids like mercury containing small particles of a ferromagnetic substance—have been further examined by Shepherd, Popplewell and Charles of the University College of North Wales, and their results are published in a recent issue of *J. Phys. D.* (**5**, 2273; 1972). Ferrofluids are of particular potential importance because they can be used as an efficient means of energy conversion; if part of a ferrofluid contained in a toroid is placed in a magnetic field and heated to the appropriate Curie temperature the whole fluid will move. It turns out that the power that can be generated in this way per unit mass of fluid depends on the square of the change in magnetization with temperature (dM/dT) and on several other parameters such as the Curie temperature.

Shepherd and his colleagues have made ferrofluids containing particles of iron–nickel alloys of various compositions. In most cases the largest of the particles were of order 1,000 Å, and the concentrations were 1 to 2 per cent by weight. Their method of making the ferrofluid is electrolytic, and utilizes a mercury cathode and an electrolyte of ferrous nickel ammonium citrate of the appropriate composition for the alloy required. Magnetic measurements on several Fe-Ni ferrofluids at 77 K showed that the coercive force for a fluid of a given particle concentration and composition passes through a maximum as the current density used in the electrolytic cell is increased. Shepherd *et al.* conclude, however, that the maximum is not attributable to an increase in particle size such that the particles contain more than a single domain; rather, it is a consequence of variations of size and shape in an essentially single-domain region.

COMPUTERS

On-line in the Lab

from a Correspondent

COMPUTERS, it need hardly be said, are, or ought to be, the experimenter's best friends, for they collect data, work out results, and, better still, run apparatus. Nevertheless, how to choose a computer, how to link it to an experiment and how to use it to best advantage remain questions to which answers are far from obvious. Faced with such problems the research worker will benefit from the experiences of other scientists who have taken the plunge and are now engaged in computer-linked experimentation.

Such a communication exercise between current users and prospective users of laboratory computers was the chief purpose of a conference organized by the Electronics and Computational Physics groups of the Institute of Physics and held on January 3 at Imperial College, London.

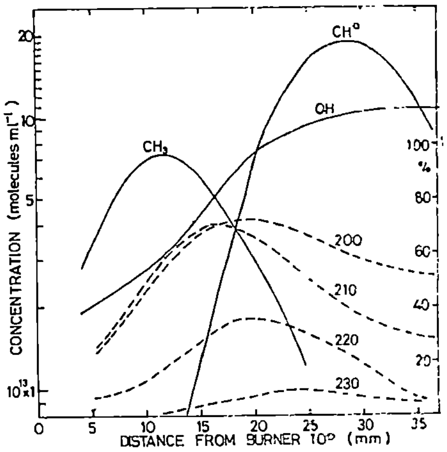
The special features of the conference included an audience which, although non-expert as far as computer applications are concerned, consisted of trained scientists; contributions solely from "users", thereby excluding parties

Methyl Radicals in Flames

RELATIVELY little is known of the exact way in which methane flames burn, except that methyl radicals are involved. Their concentration, however, is known in only the most approximate terms, chiefly because of the difficulties of applying mass spectrometry to the problem.

In 1960, Gaydon *et al.* (*Proc. Roy. Soc.*, **A256**, 323) first used absorption spectroscopy to detect the ultraviolet absorption of methyl radicals at 216 nm and to calculate at least an upper limit to the methyl radical concentration. In next Monday's *Nature Physical Science* (January 29) Harvey and Jessen report that they have used improved absorption techniques to detect strong absorption at 216 nm in several types of flame. They burned methane, ethane, propane, ethylene and acetylene at pressures of about 4 torr and gas flow rates of about 10 l. min^{-1}.

In order to make the study of the distribution of the methyl radical concentration within the flames more simple, Harvey and Jessen diluted the flow of hydrocarbon and oxygen with 3 l. min^{-1} nitrogen. What they found is shown in the diagram. It also turned out that there is another absorption feature at 212.5 nm in the flame spectrum; this is presumably part of the methyl spectrum. Unexpectedly, Harvey and Jessen find that the methyl radical concentrations are roughly the same (1 in 10^2 to 10^3) in the other hydrocarbon flames examined. In acetylene, for example, they say that their results are consistent with the occurrence of the reaction $C_2H_2 + OH \rightarrow CH_3 + CO$ possibly among others.



———, Concentration of CH_3 and OH and intensity of CH emission at 430 nm (arbitrary units); — --- —, variation of continuous absorption at various wavelengths (nm).

with some possible self-interest, such as manufacturers of equipment; and the division of the meeting into two distinct activities, namely, a survey session, with three contributions, intended to set the current scene, and a series of "case studies"—short contributions in which successful applications of on-line methods in a variety of disciplines were presented.

In a comprehensive review of the present range and facilities of mini-computers—defined as machines possessing input/output channels and "interrupt" (externally initiated program branching) capabilities — D. Turtle (Electrical Research Association) drew attention to the future potentialities of the range of microprocessors which may, before long, provide special purpose systems at a cost of around £1,000 or less by contrast with the present costs of small computer systems which run, typically, from around £8,000 for a machine with two registers, an eight-bit word, and sixteen input/output channels to perhaps £30,000 for one with sixteen registers, a twenty-four-bit word, and 256 input/output channels.

With the universal use of large-scale integrated circuits and the introduction of new, fast and cheap semiconductor random access and read only memories the possibilities for further reductions in cost and increases in systems capability are by no means exhausted. At one end of the spectrum the system of the future will be characterized by an arrangement in which all component systems (central processor, input/output processors, special arithmetic units, fast and slow stores) will communicate directly with each other, so that many processes may be carried out simultaneously. At the other end, small microprocessors, specifically designed for each application and comprising a few integrated circuits on a single circuit board, will be powerful enough to exert a supervisory and controlling function for many types of experiments.

The problems of physical interconnexion of apparatus and computer, which were considered by J. M. Richards (Computer Analysts and Programmers), offer a choice of two solutions: direct interfacing to the computer's input/output channels for maximum data transfer rates, or use of an intermediate standard interface system. The universality of the latter approach, pioneered by the nuclear physicists and resulting in the internationally standardized CAMAC system, makes it attractive to anybody who can accept the small reduction in the rate of data transfer. One of the benefits of standard interface systems lies in the relative ease with which an experiment can be transferred from one computer to another.

Having successfully linked his apparatus to his computer the experimenter still has to write his program, for he will rarely be content to use a manufacturer's application package (even if he can afford it). By means of an elaborate flow chart E. G. Murphy (UKAEA) gave guidance about the many choices now open. Only a few years ago use of assembler language was virtually compulsory, but now alternative approaches have become available to the experimenter. The choice of a good operating system and a realistic assessment of the maximum data rates required are all-important in this area.

In the session of case studies C. Derrett (MRC Air Pollution Unit, London) presented an attractively simple approach to the use of an instrument-linked computer system by non-specialists, based on an extension of the well known and simple BASIC programming language to include peripheral handling routines by means of simple CALL statements. At the opposite end of the spectrum of complexity stood two contributions from UKAEA staff at Culham describing a large data acquisition system, and the monitoring and control of a fusion experiment.

The meeting, which attracted more than 200 participants, illustrated clearly that the day when some kind of computing apparatus will form part of almost every experiment is rapidly approaching. In the meantime there seem to be many scientists who, having become convinced on-line experimenters, are willing to let their experience help those who have yet to take the first step.

PLATE TECTONICS

Thickening Lithosphere?

from our Geomagnetism Correspondent

WITH the publication of some new comments and calculations by Forristall (*J. Geophys. Res.*, **77**, 6407; 1972), the search for the most plausible plate tectonic mechanism can be said to have taken another small step forward, although, as Forristall himself freely admits, some may feel it to be a step backwards, or at least sideways. This is not because he has returned to some mechanism now discredited by geophysicists; on the contrary, he supports the plausibility of the newest idea of all —active, as opposed to passive, lithospheric spreading. The problem is that the plausibility seems to require variability in the thickness of the oceanic lithosphere, an idea which Forristall feels is "certain to be controversial".

According to Forristall's definition, passive spreading is the old mechanism whereby the lithosphere is carried along by convection in the softer asthenosphere below. In this case the velocity in the asthenosphere must increase for some distance below the lithosphere-asthenosphere boundary in order to produce the shear stress necessary to move the lithosphere along. One problem with this is that the resulting high aspect ratio cell is unlikely to be stable; and yet convection extending into the lower mantle, although not entirely discredited, also has its problems. Active spreading, on the other hand, assumes the lithosphere itself to be the prime mover, the driving force being the gravitational forces at elevated ridges or, alternatively, at the descending litho-

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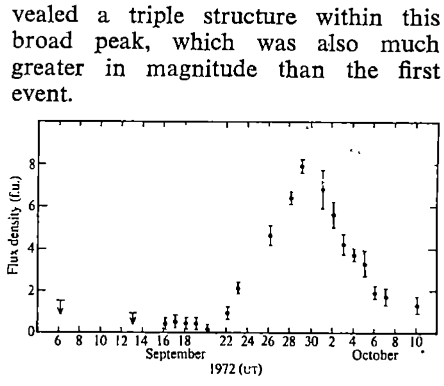
More About Cygnus X-3 Radio Flares

SINCE the great radio flares of Cygnus X-3 in September and October last year, radio astronomers have kept a watch on the source for more unusual events. These have not as yet materialized. But as a result of the quiescent state of Cyg X-3 since October, Lequeux *et al.* have been able to carry out absorption measurements at 21 cm which establish a reliable lower limit on the distance to the source. The same team carried out similar measurements during the flares; but the work described in next Monday's *Nature Physical Science* (January 29) provides the first proper base line for measurements of this kind, because the observed properties of Cyg X-3 during the flares can hardly be regarded as typical. From these measurements of the absorption between the Earth and Cyg X-3, it is clear that the source is at least 11 kpc away, although it is not clear whether it lies inside or beyond the spiral arm of our Galaxy which lies at about that distance in the same direction.

Also in next Monday's issue, Bash and Ghigo present observations of the historic flares themselves, at 365 MHz. These show the full extent of the second and larger flare, which lasted for more than two weeks (see diagram). More detailed observations have revealed a triple structure within this broad peak, which was also much greater in magnitude than the first event.



Second flare of Cygnus X-3. Observations at 365 MHz.

sphere. Either way, there must be a viscous drag from the asthenosphere which resists lithospheric motion.

On the face of it, active spreading seems unlikely, partly because the relatively thin lithosphere is required to transmit horizontal stresses over long distances and partly because of the difficulty in finding the force which produces the return flow in the asthenosphere. In addressing himself to the first of these problems Forristall notes McKenzie's point (*Geophys. J.*, **18**, 1; 1969) that tensile stresses are not required in the case where motion is caused by the descending lithosphere, but nevertheless uses them as a limiting condition in calculating the no-failure point in the lithospheric plate.

To be more specific, Forristall considers a model in which an elastic lithosphere, susceptible to failure according to the Mohr-Coulomb law, overlies a Newtonian asthenosphere. As the denser lithosphere descends into the less dense asthenosphere, the motion produces a relief of horizontal stress at the leading edge of the horizontal part of the plate and boundary stresses on the plate. What this stress relief means is that it is no longer valid to envisage the sinking plate pulling the rest of the lithosphere with it; it is the normal hydrostatic pressure at the trailing edge which pushes the plate towards the trench. Another consequence is that near the trench the horizontal principal stresses are lower than the vertical stresses.

In a series of stress calculations, Forristall then determines how great the stress relief can be without causing a failure in the plate. It turns out that, for horizontal stress relief at the leading edge of the horizontal part of the plate, the shear stress along the base of the lithosphere is constant. And because this shear stress arises from viscous drag, it can be related to the viscosity of the asthenosphere, given the vertical velocity gradient beneath the plate (actually calculated from the Navier-Stokes equation). What this means is that the no-failure condition for a lithosphere of any given thickness can be stated in terms of the maximum value of the asthenosphere's viscosity at any given asthenospheric thickness. Of course, the viscosity and thickness of the asthenosphere are not known with any certainty and so exact solutions are not possible. But by comparing his relationships with the viscosity and thickness values determined from the uplift of Fennoscandia (leaving aside the question of whether the behaviour of shield areas is really relevant to the suboceanic situation), Forristall concludes that to prevent lithospheric failure the asthenosphere must be less than 300 to 400 km thick; in other words, active spreading is only possible under this condition.

The problem of the driving force causing the return flow in the asthenosphere is less tractable and seems to require what really amounts to an *ad hoc* solution and at least one *ad hoc* rationalization. It is easy enough to calculate from Forristall's analysis the value of the required pressure gradient, but less easy to discern its physical nature. Forristall postulates that the lithosphere thickens towards the trench, producing a horizontal pressure gradient beneath it. But a thickening of the lithosphere implies an excess mass and hence a large positive gravity anomaly. The observed gravity anomalies at trenches are certainly not large enough for Forristall's purpose, which leads him to speculate further that the excess mass is compensated by a mass deficiency lower in the mantle. One possibility here is that the asthenosphere extends to greater depths in trench regions.

As an example of the magnitudes involved, Forristall considers the lithospheric thickening necessary if the density contrast between the lithosphere and asthenosphere is 0.06 g cm^{-3}. If the thickness (x) of the lithosphere at the ridge is 20 km and the thickness (y) of the asthenosphere (assumed constant) is 200 km, the lithosphere must thicken to 180 km at the trench. For $x=50$ km and $y=200$ km, the lithosphere must be 250 km thick at the trench. And if $x=20$ km and $y=150$ km, the plate must thicken to 95 km. In other words, the required lithospheric thickening is far from trivial, although it is relatively smaller the thinner the asthenosphere.

Explaining the Spectra of Heavy Cosmic Rays

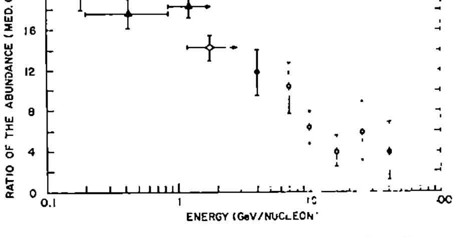
FOUR communications in next Monday's *Nature Physical Science* (January 29) discuss and supplement the evidence that there are relatively more heavy cosmic ray nuclei—iron for example —in the cosmic rays impinging on the Earth's atmosphere at energies of several tens of GeV per nucleon than at lower energies.

The situation is summarized in the diagram, which shows some of the data obtained by Ormes and Balasubrahmanyan as closed points. What they have done is to fly a balloon carrying detectors to measure particle charge and energy near the top of the atmosphere for 16 h. The remainder of their data comprise the differential spectra of several nuclei and groups of nuclei at energies greater than 3.3 GeV per nucleon. They conclude that the so-called secondary nuclei (that is those formed chiefly by the fragmentation of iron and nickel interacting with interstellar hydrogen) have somewhat steeper energy spectra than the cosmic ray "source" nuclei (chiefly iron and nickel). If these spectra continue to higher energies, say Ormes and Balasubrahmanyan, iron will become the most abundant nucleus apart from protons and helium nuclei at around 200 GeV per nucleon.

Although Ormes and Balasubrahmanyan draw some conclusions from their results, it is the other three groups of authors who delve deeply into the ramifications of the spectral differences between heavy and light nuclei for theories of the origin and acceleration of cosmic rays. Webber, Lezniak, Kish and Damle consider an equilibrium model for cosmic ray production and leakage from the Galaxy in which the "escape length" is assumed to be a function of energy. They find that a dependence of E^{-1} fits the energy variations of both ratios (C+O)/(Fe+Ni) and (Nuclei with $Z=$ 17–25)/(Fe+Ni). On the other hand, such a strong dependence on E does not seem to be reflected by the ratio of the number of Li, Be and B nuclei (thought to be secondary nuclei) to the number of C and O nuclei (primary nuclei). The question of the energy dependence of the theoretical term which describes the probability that galactic rays leave the Galaxy is also considered by Audouze and Cesarsky.

In the final communication Meneguzzi comes to the conclusion that the energy dependence of the abundance ratios is consistent with a decrease of the cosmic ray escape length from about 7 g cm^{-2} at about 2 GeV per nucleon to less than 1 g cm^{-2} at 100 GeV per nucleon. He rejects the need for additional assumptions like a dependence of the mean free path on charge or a charged dependence of the spectral index of the source.

As Audouze and Cesarsky point out, many of the data now available seem to upset the theories that require cosmic rays to be confined to the disk of the Galaxy.



Ratio of abundance of "medium" nuclei ($6\leqslant Z\leqslant 9$) to those in the iron group ($23\leqslant Z\leqslant 28$) as a function of energy per nucleon.

X-ray Star Problems Defined

by our Cosmology Correspondent

AT a specialist meeting of the Royal Astronomical Society on January 12, problems raised by the discovery of X-ray sources in binary systems were placed in the perspective of the latest observations at radio, optical and X-ray wavelengths. Few detailed answers to these problems have yet emerged; but theoreticians are now learning which questions must be answered by the observations in order to differentiate between those models which are at present plausible.

The first speaker, Dr K. A. Pounds (University of Leicester), described some of these observations at X-ray frequencies—not, this time, the work of his own group, but chiefly the Uhuru observations. He reported that American Science and Engineering are now preparing the third Uhuru catalogue (3U) which will include some 200 sources, down to an intensity 10^{-3} times that of the Crab. It seems that these 200 sources are divided almost equally between galactic and extragalactic objects. Of the galactic sources, the binary systems which are arousing so much interest form a subset of six in our Galaxy and one in the Small Magellanic Cloud.

Several of these sources show a rapid variation with a period of a second or two (reminiscent of pulsars) superimposed on a binary period of hours or days. One of the most interesting results to emerge from extended observations during the past few months is that in some cases at least this rapid variation is speeding up. Her X-1, for example, has a "pulsar" period of 1.2 s and a binary period of 1.7 day; the former now seems to be increasing by 4 μs in six months, according to recent MIT data which Dr Pounds reported.

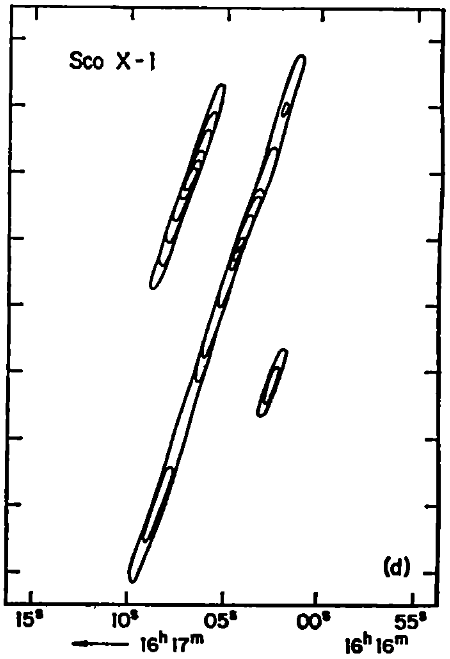
Two of the sources have been studied in detail by optical astronomers. Dr P. Murdin (Royal Greenwich Observatory) described these studies of Her X-1 and Cyg X-1—which have received this concentrated attention, of course, simply because of the lack of reliable optical identifications of the other sources. Her X-1 has been identified with HZ Her, a 14 mag star which shows the same binary period of 1.7 day as the X-ray source. The primary in the system seems to be affected by the X-ray emission of the companion, but a reasonably comprehensive model has been proposed by Forman *et al.* (*Astrophys. J. Lett.*, **177**, L103; 1972; see also *Nature Physical Science*, **240**, 169; 1972). At X-ray frequencies, the source also shows a regular 35-day variation, which has yet to be explained, and there is marginal evidence for optical variations at the "pulsar" period.

Cyg X-1, however, is the joker in the binary X-ray star pack. As Dr Murdin put it, this is "something completely different". This optical identification was achieved by a roundabout route, which verges on being a circular argument. Early last year, the emission of the source in different X-ray channels changed abruptly; at the same time, a new radio source appeared in that part of the sky, and the radio position is good enough to permit identification of the radio source with a BO supergiant. There is no direct reason to connect the X-ray source with either the star or radio source, but the coincidence of the sudden change in X-ray properties with the appearance of the radio source is so strong that nobody has seriously questioned the identification of Cyg X-1 with the BO supergiant. This is the source which many theorists have turned to as evidence that black holes exist. Dr Murdin stressed, however, that although the source is clearly unusual, and asymmetry in the light curve implies that the stars in the system are non-spherical, the optical data are consistent with the view that the secondary is an early main sequence star. There is no pressing need to invoke the "counsel of desperation" hypothesis that there is a black hole in the system. Black holes, he says, are a solution looking for a problem.

In discussing the radio properties of these objects, Dr G. K. Miley (Westerbork) concentrated chiefly on the remarkable outburst of Cyg X-3. Most of the work described has already appeared in *Nature* (see special issue of *Nature Physical Science*, October 23, 1972). But one interesting possibility which Dr Miley pointed to is that the triple radio source associated with Sco X-1 might have originated in an explosion similar to the event recently observed in Cyg X-3. Other than Cyg X-3 at the time of the two flares, all these binary X-ray systems are weak or non-existent radio sources; only Cyg X-1 and Cyg X-3 are firmly identified at radio frequencies, and, although Sco X-1 may be of the same family as Cyg X-3, no one consistent model will explain the observed properties of all three objects.

It was left to Professor Martin Rees (at present at the University of Sussex but shortly to return to Cambridge as Sir Fred Hoyle's successor as Plumian Professor) to discuss the theoretical problems—not, he was quick to point out, to provide the answers to the questions raised by the observations. It seems that the overall features are happily explained by a model in which a giant star has a magnetic neutron star companion. Under those conditions, slight mass loss from the giant—even a strong stellar wind—can cause enough matter to accrete onto the neutron star to produce the observed X-rays, because as much as 10 per cent of the rest mass energy of the infalling matter is liberated as it falls down the neutron star's potential well. The mechanism is not unlike that of a pulsar in reverse, for pulsars are generally believed to be losing matter by outflow along lines of magnetic force. Professor Rees suggested that this could be why X-ray "pulsars" are seen in binary systems, where there is infalling matter, but radio pulsars are found only in isolation. Also, transfer of angular momentum by the infalling matter should cause the neutron star to spin faster, in agreement with the latest X-ray observations.

The detailed answers to the many problems raised at this meeting remain to be found. Why do the X-rays in these sources sometimes "switch off" for days at a time? Why do the optical variations show no similar behaviour? How did these binary systems evolve to their present state? Is there a black hole in Cygnus X-1? And in addition searches of survey plates show that the optical variations of Her X-1 sometimes switch off for years at a time. This raises the number of time scales associated with that source, at least, to four. But the problems are not insoluble; their number simply indicates the vigorous growth of this new branch of astronomy.



Sco X-1 mapped at 2,695 MHz (after Hjellming and Wade, *Astrophys. J. Lett.*, **164**, L1; 1971). Could the triple structure—smeared in this figure by the antenna response—be the result of an outburst like that recently observed in Cyg X-3?

Is Polio a Model for Consumer Research?

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Dr Wyatt considers to what extent the customer-contractor principle was at work in research on poliomyelitis.

In the discussions of the Rothschild proposals for financing applied research, there has been little attempt so far to examine previous case histories to see if the formula has worked in the past. Nor has the relation of pure or basic to applied work been examined: if, as suggested by the research councils[1], much of their basic work is funded for its relevance to specific ends, then much of the controversy would seem pointless.

The control of poliomyelitis is a cautionary tale, successful though the outcome may have been. There were four clearly defined phases. From about 1880, when poliomyelitis was first recognized as a problem, until 1934, research was carried out by individuals financed from a variety of sources. The production of a book on poliomyelitis[2] marked the beginning of more deliberately directed effort. In 1934 a consumer-directed body, the President's Birthday Ball Commission, funded, among other work, applied work on a vaccine. The Commission was replaced in 1938 by the National Foundation, another consumer body, which worked through a scientific research committee in much the way Rothschild proposes. For ten years it funded pure research, for the next ten a mixture of pure and applied. How well, or how badly, did each of these systems work? And what lessons are to be learned about the control and funding of customer-directed research?

In medicine, and perhaps agriculture, practical problems must be tackled before the technical means of solving them are known. The principal cause of poliomyelitis, a virus, was discovered by Landsteiner and Popper[3] in 1909 (although this was still disputed twenty years later). But the bases for all further work were clearly shown by Wickman[4] in 1913: poliomyelitis is caused by a virus in the spinal cord, with inflammation of the motor ganglia, the disease can be reproduced in monkeys, the incubation period is probably more than 4 days, monkeys can acquire immunity (antibodies), it is an infectious disease spread by humans who show no overt disease (healthy carriers) or who have abortive attacks, insect vectors play no part in its transmission, and the virus could be recovered from the human intestinal tract. Historically, however, almost 40 years were needed before these ideas were accepted and even though immunity had been demonstrated in monkeys and the incidence of poliomyelitis was lower in adults than in children, thus suggesting the acquisition of natural immunity by human beings, the goal of a vaccine against poliomyelitis was delayed for several years. Why should there have been such a delay?

The concentration of research at one great centre, the Rockefeller Institute, was partly responsible, and the opinions of Flexner, its head, carried too much authority. As late as 1926 he and Noguchi were still claiming that a globoid body, growing in lifeless medium, was the causative agent of poliomyelitis. Concentration of research at the centre of excellence resulted in several technical errors which were not recognized until the 1950s. The MV strain of virus, which had been used at the Rockefeller, was then shown to be so adapted to monkey brain passage and so neurotropic that it would no longer grow in cells from other organs. Thus in 1936 Sabin and Olitsky had failed to grow it in tissue cultures and this was accepted until 1949 when Enders, Weller and Robbins grew it in human non-nervous tissue. The MV strain was also probably an inconstant mixture of viruses of different types. Monkeys immunized with this mixed strain were sometimes found to be susceptible to further challenge. Although Burnet and Macnamara[5] had presented evidence that there might be two antigenic types, the MV strain was still used. Also the MV strain would not infect cynomolgous monkeys by feeding.

The factors so clearly deduced by Wickman[4] from the natural disease in man were tested in the 1930s, but were obscured by the results obtained from tests involving animal models. The solution of the technical problems of infecting monkeys introduced new—and on the whole, irrelevant—ideas. One such was the theory of infection by way of the olfactory nerves, originally put forward by Flexner in 1910. Monkeys could be infected by rubbing poliovirus into the nasal mucous membrane, but this was an artificial route. It led, however, to the attempt in 1936–38 to block virus entry of children by treatment of the mucous membranes of the nose with chemicals. This was probably ineffective, was impracticable and could result in the loss of sense of smell.

On the other hand, the Rockefeller Institute, as a centre of excellence, attracted many who afterwards made such significant contributions: Herald Cox, Isabel Morgan, Sabin and Syverton all worked with Olitsky. The institute was also the home of Rivers, who later presided over the funds for polio research.

Funds for Research

In 1934 a new body, the President's Birthday Ball Commission, began to give funds for research through a scientific advisory committee. This corresponded to a consumer body: it comprised a neurosurgeon, a third vice-president of the Metropolitan Life Assurance, the director of the Hygienic Laboratory of the US Public Health Service (forerunner of the National Institutes of Health) and Dr Paul de Kruif, a microbiologist turned writer. It was not strong on science and gave most of its funds ($241,000 in 1935) for applied work on the production of a vaccine[6]. The Park-Brodie formalin vaccine was ineffective at best, and the Kolmer vaccine, a so-called attenuated vaccine, caused at least five deaths[7]. The first attempts at applied science had ended in failure because there was no sure basis of knowledge on which to rest them. But, surprisingly, the Rockefeller Institute, which had not been involved, rapidly faded from the poliomyelitis field. Whereas much of the previous work had been done in public health laboratories, the emphasis now shifted more and more to the laboratories of the medical schools. The United States government remained conspicuously absent and seemingly only intervened when things went wrong—Dr Leake, a USPHS officer after the Kolmer and Brodie incidents and the USPHS after the Cutter incident in 1955 (ref. 7).

Success of a Rothschild-type Body

In 1938 the Ball Commission was replaced by the National Foundation for Infantile Paralysis. The composition of the scientific research committee, with Tom Rivers as chairman, was less consumer-oriented and was more like that of a research council: one lay member, one government administrator/scientist, three top virologists (including Rivers) and an ex-scientist (de Kruif) as secretary. An eleven point programme[6] was adopted, in order of importance: pathology of poliomyelitis in human beings; portal of entry and exit of virus; purification and concentration of virus; what is to be called poliomyelitis?; mode of transmission of virus from man to man; transmission of virus along nerves; further attempts to establish poliomyelitis in small laboratory animals; settlement of the question of chemical blockade; chemotherapy of poliomyelitis; relation of constitution to susceptibility; production of a good vaccine. Basic science was clearly placed first, with prevention of the disease when possible.

From the outset, the National Foundation, guided by Rivers and his committee, funded work not only on poliovirus but on many other viruses and even on bacteriophage and protein chemistry (Linus Pauling). It also funded general fellowships for work and travel (J. D. Watson). The foundation also gave very large sums of money for what might now be considered wasteful duplication of work: at least three large groups on the epidemiology of poliomyelitis and the continued funding of Sabin for the work leading to his oral vaccine when the foundation was heavily committed to Salk and his inactivated vaccine.

It was Dr Maxcy, an academic, who approached the foundation for a five year grant to fund a permanent research centre at Johns Hopkins School of Hygiene to investigate the pathology and epidemiology of poliomyelitis. This led to a new concept of funding—later adopted by NIH and others. Workers at this centre laid the firm basis of pathology, showed conclusively that there were probably three types of poliovirus and produced the first effective vaccine. At the same time, the Yale unit under Paul and Trask had studied the epidemiology extensively; it was founded in 1932 and was later funded by the foundation. All this work led to a renewed interest in immunity and a possible vaccine. For fifteen years after the Kolmer and Park-Brodie fiascos, thoughts of a vaccine had been muted, but by 1950 sufficient knowledge had been gathered to bring an effective vaccine into the realms of possibility.

Up to this time, the funds of the foundation for scientific work had been given for a judicious blend of polio and related research. There can be no doubt, however, that the foundation regarded it all as "applied" research and that the recipients welcomed the chance to help fight poliomyelitis. They had faith in the foundation and the foundation trusted them[8].

With the confirmation of three types of virus, the foundation contracted its first applied work. The typing programme cost $1,400,000 and 30,000 monkeys[9] and was wholly successful: the scientists recognized the necessity for it and four groups agreed to do it. When faced with the necessity for routine, directed, and collaborative work, the research scientists responded.

In about 1953 there were at least six people or groups who had produced vaccines. Fortunately Salk was prepared and willing to proceed. He already had experience in producing a formalin-inactivated influenza vaccine, he had the large laboratory necessary and he and his staff had experience in titrating virus and antibody. Yet the research so carefully fostered by Rivers and his committee and so successfully carried out by so many scientists could only be translated into an effective vaccine after a chance technical advance. The only source for poliovirus had been from brains and spinal cords of susceptible mammals. The work of Rivers himself[10], and many others, had shown that injection of such material could give rise to experimental allergic encephalitis (EAE) in animals, and Sabin[11] had shown that some human adults gave a delayed type response to extracts of spinal cord. A vaccine prepared in monkey spinal cords would have been very costly and dangerous and nobody had attempted to purify such material. Fortunately, an unexpected technical advance made a killed vaccine possible. In 1949, Enders, Weller and Robbins, funded by a National Foundation grant for basic virology, discovered that poliovirus could replicate in human non-neural tissues[8]. A few years later a similar unexpected technical advance, also funded by the foundation, made the Sabin oral vaccine possible when Dulbecco[12] invented the plaque overlay technique and enabled Sabin to clone his virus stocks. In this case, the goal was clear but the means to it were not known.

Who Represented the Consumer?

It is not easy to see how a more firmly directed programme (consumer-oriented) could have been more successful. One can, however, see how the consumer-directed bodies planned ahead and later reacted under stress. Once it had a vaccine, the National Foundation was only with difficulty persuaded to test it scientifically[9]. The trial, conducted by T. Francis (a former foundation grantee and a mentor of Salk), was a brilliant success and a classic study. The foundation, however, felt its duty to the public overwhelming, and, unmindful of possible hazards, committed itself to mass use of the vaccine in 1955. The US government, the USPHS and the standards section of NIH were all swept along. The difficulties of manufacturing the vaccine on a large scale had not been foreseen by Salk, the foundation, the manufacturing companies or the government. When difficulties arose, Salk and the companies did not appreciate them. The government department had not the means, experience or knowledge to test the vaccines for safety or effectiveness. The presence of live virulent virus in the Cutter vaccines led to 260 cases associated with vaccine, including ten deaths[7]. In some ways it was a fortunate accident: it was large enough to be recognizable as such and to be investigated. The situation, although regrettable, was certainly less severe than it might have been if the vaccine had not been used.

As a consequence, a new Division of Biologic Standards was established at NIH in a new building, safety testing was investigated and improved, the Poliomyelitis Surveillance Unit was established at CDC and international standards approved. But I believe the accident did more—it alerted scientists to the dangers and may have helped to create a climate of opinion which led to the recognition of the dangers of thalidomide. If the vaccines had been contaminated with a much smaller amount of active virus, cases might not have been noticed and the eventual toll might have been far greater.

Each time the government should have foreseen problems or become involved, it was found wanting. In the cases of the Kolmer and Park-Brodie vaccines, the Cutter incident, the licensing of the Koprowski and Cox vaccines and the use of the oral Sabin vaccine, the government was silent or called in the scientists. In the cases where large numbers of children were involved—the nasal sprays, the field trial of the Salk vaccine and the gamma-globulin trial—the government was silent. It has been suggested that development and safety testing should be carried out by the same agency. Can one agency fulfil both functions? The development problems which must be minimized may be the ones which must be perceived for the sake of safety; the researcher has to see the wood but the safety testers must be constantly falling over the trees. In the United States the separation of role was less clear in practice than on paper, for the scientists so active in polio research were also called to advise the government on safety.

Industry might also be considered as consumer-directed: but with the exception of Lederle, the pharmaceutical houses contributed little to poliomyelitis research. A few undertook to produce the Salk vaccine: all are believed to have experienced difficulty in producing a safe vaccine, some did not produce a safe vaccine and Cutter Laboratories was sued. At Lederle, Koprowski produced an oral vaccine and conducted the first trials on humans. The vaccine was used on a limited scale but was withdrawn after Dick had claimed that he had detected a reversion to neurovirulence. A Lederle-Cox oral vaccine was later used with some vaccine-associated cases in West Berlin in 1960 (ref. 13). Sabin's oral vaccine has since been used extensively all over the world in spite of alleged vaccine-associated cases. Sabin vigorously refuted the methods and findings of those who had suggested that his strains reverted to virulence: if he is correct, the arguments would also clear Koprowski's vaccine as well. Lederle, the one commercial company to do significant research in poliomyelitis, was unlucky: the other commercial companies who produced the early Salk vaccine also made little profit.

Polio and Cancer

How much of the success of the polio story was due to the consumer-directed role of the National Foundation and how much to the vision of Rivers the scientist and O'Connor the organizer? John R. Paul gives a sympathetic picture of the National Foundation but says "the NFIP was extraordinarily lucky to have entered the arena at just the right time and to have enlisted from the start the talents of just the right man—Tom Rivers"[8]. Rivers was more than a link man between the foundation and the $69,000,000 which it spent on research, and the scientists who received it; he was also the father of American virology. But other scientists—Paul, Enders and Bodian in particular—stand out not only for their scientific contributions but also as advisers and arbiters.

Would a centre of excellence in the form of a central National Polio Institute, either USPHS or the foundation, have supplied the answers earlier or might it have exerted a baleful influence similar to that of the Rockefeller Institute? Would the USPHS have been a better source of funds than the foundation? Would contracts earlier in the programme have been more effective? How did the propaganda that brought in the money affect the responses of the scientists to work on polio rather than other viruses or diseases? Would a similar emotional appeal to the public affect the scientists' attitude to applied research now or was polio a disease with a very special appeal? With the doubling of funds directed towards a cure for cancer, these are important questions. For, by comparison with polio, cancer is still at the pre-1909 stage.

Whatever the answers to these questions, scientists worked willingly on the consumer-directed research for prevention of poliomyelitis and much of the impetus came from the scientists themselves. Maxcy had come forward with the idea of a team of workers at Johns Hopkins; he also proposed group cooperation for typing. The impetus for the germinal round table conferences came from the scientists and from Dr Weaver, a scientist who became director of research at the NFIP. These conferences were very successful and the tradition has been carried on by the National Cancer Institute. In spite of the overall direction from the foundation, it was individual scientists who unexpectedly provided the key ideas—Dulbecco with the isolation of single viruses, Enders, Weller and Robbins with tissue culture, Koprowski and Sabin with their attenuated viruses.

Yet, curiously, three of the fundamental problems listed by the scientific research committee were never satisfactorily solved—(1) pathology of poliomyelitis in human beings, (4) transmission of virus along nerves, and (10) relation of constitution to susceptibility. The technical problem of prevention of poliomyelitis was solved in a way which bypassed these fundamental problems. Could it be that cancer will prove susceptible to technical solution without a scientific resolution?

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Empiricism and Phenomenology

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Mr Sadler presents his reactions to an article in *Nature* by Dr R. A. Crowson on science and phenomenology.

I SUGGEST that the article by Crowson[1] expressing his strong sympathy for phenomenology does not provide a vindication for the conclusion that phenomenology provides "satisfactory basic orientations for psychologists, historians, moral philosophers, politicians" or natural historians. Much of the weakness of Crowson's article lies in the introduction of vague concepts in support of arguments which require considerable clarity and precision if the problems are to be formulated and tackled.

What, for example, could count as "satisfactory basic orientations"? His extreme emphasis on heuristic potential needs some justification. Similarly, the notion of "the most essential reality" is far from transparently obvious. As a starting point, I would claim that the purpose of pursuits like science and philosophy is to increase our understanding of the world and to help clear up puzzles. I hope that this much can be accepted as quite basic and not subject to exceptions.

With someone who prefers an incoherent picture of nature, I have no idea how to proceed—just as in meta-ethics, one is powerless to proceed with someone who regards a universe without sentience as possessing greater intrinsic value than one with sentience.

Beliefs of Natural Scientists

It may well be that Crowson is reporting correctly when he writes that leading phenomenologists regard natural scientists as committed to the belief that the most essential reality can and should be expressed in abstract mathematical formulae. If this is what leading phenomenologists believe, then they should conduct their sociological surveys more carefully.

To start with, it is not true that there is one precisely formulated philosophy of science held by all natural scientists. The most that can be said is that many philosophically inclined natural scientists subscribe to some form of empiricism. The criterion of verifiability for meaningfulness is popular, and one thing a logical positivist could not say is that he believes that the most essential reality can and should be expressed in abstract mathematical formulae.

The historical causal genesis of this sort of expression may be due to a line of thinking suggested by Eddington, according to which we cannot, given a realist interpretation of modern physics, suppose that tables and chairs are "really" hard solids possessing smooth surfaces, because tables and chairs are composed of molecules, which are composed of atoms, which in turn have a fine structure and, if we continue our picture thinking and accept the Copenhagen interpretation of quantum mechanics, we are left regarding variables in our state equations as the square root of a probability density function. This line of reasoning relies for its appeal on the gross misuse of words. It assumes that because the predicates "hard", "solid" and "smooth" cannot meaningfully be predicated at the micro-level when used with their ordinary meanings, they cannot be correctly applied to macroscopic objects like tables and chairs. It is surely reasonable to reject this assumption[2].

I do not wish to suggest that the relation between mathematics and physics is transparently obvious. Husserl, who had received some mathematical training, went to some pains to refute J. S. Mill's view that mathematical knowledge is based on empirical generalization. Some modern empiricists regard mathematical knowledge as analytic *a priori*. Nevertheless, I think Quine[3] is correct to emphasize that the analytic-synthetic distinction is not completely sharp. Our concepts have theories built into them from the start. Our fundamental physical laws are like the principles of mathematics and logic to the extent that they cannot be overthrown by isolated experiments. It is always possible to retain the laws and explain our results in a more or less *ad hoc* way. Furthermore, this is surely the reasonable approach to take for as long as no acceptable alternative theory is available.

The role of the conservation of energy in modern physics is a case in point. We cannot today describe any experiments which would overthrow it, although the law is not analytic and might be abandoned if there were good theoretical reasons for doing so and positive supporting experiments[4].

It would seem central to both Sartre and Husserl to get "back to the things". It may well be the case that our brain structure is such that it leads infants to hypothesize one of a limited number of types of grammar[5]. This offers, however, no support for mapping the subject-predicate structure of the natural Indo-European languages onto world structure.

In any case, in Chinese, so I am informed, the very notion of substance does not occur, because the language is not of subject-predicate form. As the grammar of our language reflects a conceptual scheme, it is clearly related to the issues of theory neutrality. The natural European languages use nouns, adjectives, and so on, whereas an artificial language uses such things as quantifiers, variables, and predicates. Many of the puzzles which arise in Meinong and Husserl can be dealt with by adopting an adequate "theory of descriptions"[6,7], that is, very briefly, "The golden mountain does not exist" ceases to be puzzling when presented symbolically as: (x)—(x is golden and x is mountainous), or more loosely in colloquial usage: "There is nothing which is both golden and mountainous".

Even if, somehow, the study of neurophysiology and psycholinguistics should eventually lead us to the conclusion that our innate brain structure is such as usually to cause us to formulate our ordinary conceptual schemes of substance and change, this only leads to the conclusion that these conceptual schema have, until now at any rate, provided good survival value, and not that they are metaphysically basic.

It often happens that an incorrect theory is more practically useful than a correct one. Commonsense language may merely be a convenient bridge to the development of a more adequate scientific language using quantification theory and the concepts of four-dimensional space-time objects rather than three-dimensional objects evolving in time.

On Contingency

Crowson wishes to focus attention on the notion of contingency. Colloquially, one describes a state of affairs as contingent if it may or may not happen. More precisely, a logically contingent statement is contingent with respect to the laws of logic, for example, the truth value of "p v q" is contingent on the truth values of "p" and "q". A physically contingent statement is contingent with respect to the (assumed known) laws of nature. It seems odd for Crowson to write: "Natural philosophers tend to consider everything which is not a strictly conducted experiment in a laboratory as contingent". The function of strictly conducted laboratory experiments is to create information—and clearly this they cannot do unless they are contingent. No information is gained from the result of an experiment if the result could not have been otherwise. It is easy to illustrate this point further by referring to an article in *Nature*[8], which was accompanied by the publishing of the referee's report. The first sentence of the article asserts that experiments have shown that the velocity of light is independent of the velocity of the source to a high degree of accuracy. The referee comments that from a relativistic point of view, the possibility of dependence of the velocity of light on the velocity of the source does not arise because the independence is a tautology. The referee goes on to deplore that after half a century of relativity, physicists should still think in terms of (quasi) Newtonian concepts.

In metaphysics, contingency is the opposite of determinism, that is, it is held that some events are uncaused. It would seem that it is this metaphysical sense of contingency which is accepted by phenomenologists. To regard the principle of causality as an empirical generalization in the manner of J. S. Mill can be shown to amount to merely giving an implicit definition of what it is to be a determining factor[2]. It is a historical fact that the enterprise of natural science has proceeded by accepting determinism as at least a methodological rule for enquiry. As an overall view, many natural scientists would seem to take a soft determinist line. Even for Sartre, the attempt to rationalize the world is rejected. Exactly this point had already been covered in traditional British empiricism which maintains that "brute factuality" cannot be explained away as necessity in disguise. The general objective of theoretical science is to achieve deterministic explanations governed by laws, that is, given an initial state of the system, the explanatory theory logically established a unique state existing at any other time. This general formulation has the advantage of not prescribing a particular definition for the state descriptions, that is, statistical or quasi-statistical state variables are acceptable. It is logically possible that men could have sought to understand their environment by adopting a different maxim for enquiry—the principle is not a synthetic *a priori* truth. Thus, the acceptance of the principle of causality as a maxim of enquiry is an analytic consequence of what is commonly meant by natural science.

Natural Science and Natural History

I further maintain that there is no very deep distinction between natural science and natural history. The drawing of a deep difference dates back at least to the time of Aristotle. He regarded natural science as "more philosophic and of graver import" than history, as the latter is concerned with the special and singular. This *prima facie* difference, however, needs examination. It can, I think, be agreed that natural history is concerned with particular facts about our terrestrial environment; palaeontology, for example, is concerned with the relating of a historical narrative. Also, even though geology makes use of very general physical laws for explanation of particular facts, this does not detract from its status as history, for its chief concern is with the particular facts themselves and not with particular facts regarded as tests of physical laws. Thus, a geologist doing a radiometric survey of some minerals is not concerned with the physical basis of β decay. As regards to the natural sciences, however, it is worthwhile to emphasize that their general statements cannot be asserted as empirically warranted except by establishing and using singular statements. Kepler formulated his laws to apply only to the solar system. The extension to any system of bodies gravitating under an inverse square law is a generalization. Similarly, we could suppose it to be a biological law that a leopard cannot change its spots. When this is expressed in the form: (x) (x is a terrestrial leopard $\supset$ x cannot change its spots), it is true everywhere. The detail of biological evolution on our planet is a study in terrestrial history. Nevertheless, it would seem a legitimate function of biologists to concern themselves with propositions about evolution, which are more general in the sense that they are applicable anywhere and at any time in the universe, for example, the statement that carbon is essential to any life form may be true, or it may be false. It would be interesting to know which[9–11].

Other Points

The remaining points of Crowson's article I shall deal with very briefly. Empirical ethical theories have been influential at least since the time of Bentham. The manner in which shape words, lens-shaped, grooved, and so on, which are deliberately vague are accounted for within the framework of a fairly orthodox empiricism, is discussed by Hospers[12]. Bergson's theory of time has some romantic appeal, but little else to recommend it. I do not think that Husserl's theory provides any trouble for an identity theory of mind (central state materialism). When one says: "I am thinking about the Melbourne Cup", only a rough similarity of abstract structure of brain states and the physical event, which is the horse race, is required. There are various discussions of the intentionality of our thoughts in ref. 4.

One point of methodology in which Crowson acquiesces seems to me particularly undesirable. He would wish to claim that while phenomenology is an appropriate belief for natural historians, it is not (at present at least) appropriate for natural scientists. (In fact, at least one quite eminent mathematical physicist was, at one time, influenced strongly by Husserl's phenomenonology[13].) To take this line seems to me to give up too easily. I would judge the attempt to see the world as a complete whole to be worthwhile for its own sake.

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Dr Crowson replies:

SADLER's comments on my article on science and phenomenology provide almost a textbook example of the mutual misunderstandings which are liable to affect communications between practising scientists on the one hand and formal philosophers on the other. Sadler writes in the manner of a professional philosopher, judging ideas by current academic standards of logical coherence. In this sphere, he is no doubt much better qualified to speak than I, and it would be very rash of me to try to criticize his logic. My article was, however, written—though perhaps this was not made sufficiently clear at the time—from the point of view of a natural historian, after seeking in the writings of various schools of philosophy for a fundamental intellectual attitude which could be reconciled with his own intellectual practices and experience. In the domain of natural history (which is more fully defined and discussed in ref. 1), I have considerable experience and may well be better qualified to draw general conclusions than is Mr Sadler.

One point of agreement between us is that, in his phenomenology, Husserl tried to reassert the fundamentality of perceived things as opposed to mental schemata; this attitude would tend to link Husserl with natural history rather than natural philosophy. Sadler maintains, however, that "there is no very deep distinction between natural science and natural history"; Aristotle is cited for the opinion that natural science is "more philosophical and of graver import" than history. For the Stagyrite, however, history would have meant human history only, and natural science would have included natural history, so that the quoted opinion is strictly irrelevant to this discussion. Sadler, incidentally, never makes it quite clear whether his "natural science" is equivalent to my natural philosophy.

The most difficult issues involved in the differences between us are concerned with contingency. The concept of the contingent seems to be present in one form or another, more often implicitly than explicitly, in most previous philosophical systems, although I have yet to read a work which provides a satisfying definition and treatment of it. Sadler's colloquial definition, that an event is contingent "if it may or may not happen", is probably as useful as any of the more elaborate ones I have seen. According to anti-historicist philosophers like Karl Popper, the whole of (human) history is a catalogue of contingencies, so defined. It would be a logical extension of the Popperian attitude to apply it also to the entire domain of organic evolution and its products, comprising the subject matter of virology, bacteriology, botany and zoology. In most academically respectable philosophical systems, to refer any phenomena to the realm of the contingent is to banish them to a sort of limbo, where no philosophical significance is to be found.

For positivists, Cartesians and similar schools, the whole domain of natural history is liable to be equated with that of contingency, and thus to be excluded from serious philosophical consideration. Sadler deplores my suggestion that no formal philosophical system yet proposed, which would satisfy his canons of logical coherence, could provide an adequate intellectual basis for all types of human activity, scientific, artistic, moral and political. Regrettable or not, this seems to me to be a plain statement of fact, exemplified by the failure of current scientific philosophies to attribute any philosophical significance to natural history. It is entirely characteristic that the name of Charles Darwin, and the topic of organic evolution, make no appearance in the index to *The Logic of Scientific Discovery*. I agree with Sadler in wishing that we could all share a universal philosophy, but suspect that, if such a philosophy ever comes to exist, it will violate some of his canons of logical coherence.

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Trace Elements in the Atmospheric Environment

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The origins of atmospheric trace elements measured in the vicinity of Lake Windermere are indicated by relationships derived between the levels in air, rain and dry deposition.

TRACE elements in airborne dust arise from the Earth's surface and also descend from sources beyond the atmosphere[1]. The terrestrial aerosols are raised from the surface of land and ocean by winds, by the eruption of volcanoes and by industrial activities.

Larger particles (>10 μm) will promptly return to the surface by sedimentation, but smaller particles may be raised by updraughts and turbulence to higher altitudes, so that dispersal is more widespread; particles reaching the stratosphere will eventually be distributed on a worldwide scale: those that remain in the troposphere will be transported in the zonal circulation before returning to the Earth's surface[2]. Aerosols are transferred to the Earth's surface by wet deposition through precipitation and by dry deposition through sedimentation, impaction and diffusion[3].

Trace elements in the atmosphere, in the ground and in water can be considered in three roles: (*a*) as nutrients, (*b*) as potentially toxic pollutants and (*c*) as tracers of transfer mechanisms. It is necessary to determine the background levels of trace elements and the natural and unnatural variations about these levels, to observe the passage of the trace elements through the environment. It follows that knowledge is required of the transfer mechanisms of trace elements between air, rain, water, vegetation and so on, and of the corresponding deposition inventories. Other analyses of the atmospheric environment have often been restricted to trace elements in air, to urban areas or to short sampling periods[4-14]. Less information is available on the composition of rainwater[15-20].

The present exploratory programme of environmental analysis was established to determine the levels and immediate fate of atmospheric trace elements at a single location. The programme was sponsored by the Natural Environment Research Council, who selected a relatively unpolluted site near Lake Windermere (Westmorland) for the measurements in the field. Since April 1970, there has been continuous sampling, using weekly or monthly periods, not only of airborne dust near ground level but also of rainwater, and from November 1970 samples of the dry deposition have been collected as well. Samples have been analysed for about 30 trace elements.

The site chosen for sampling is at Wraymires (grid reference SD362974), 84 m above sea level and with an annual average rainfall of 180 cm. The nearest heavy industry is 30 km towards the south-west, at Barrow-in-Furness. The methods of sampling were made simple in order to obtain continuous and trouble-free operation in a remote area. Samples of airborne dust were collected by drawing air through filter papers held in polypropylene ducts. Rain was collected in a polythene funnel and bottle, which would contain the total deposition—that is, the wet deposition plus the dry deposit on the funnel that was washed in by subsequent rain. Dry deposition was collected on a horizontal sheet of filter paper sheltered beneath a plastic cover to shield the surface from rain. Most of the trace element analyses were made by neutron activation of the sample followed by gamma ray spectrometry[21-24], although for lead, nickel and cadmium, for example, X-ray fluorescence has proved convenient and economical[25].

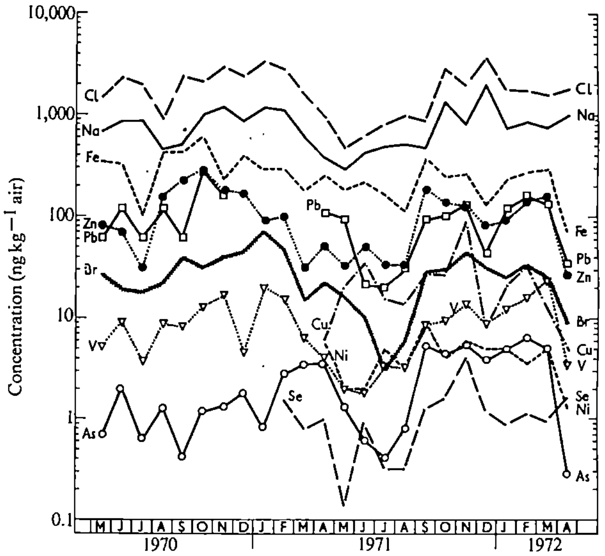

Fig. 1 Elemental concentration in air near ground level at Wraymires (1970-72).

Composition of Deposits

Some 30 elements have been determined quantitatively in aerosol samples from Wraymires, either as weekly or monthly concentrations. In addition, nine other elements have been qualitatively identified. The highest concentrations have been ~ 1 µg kg^{-1} of air, in the case of Cl, Na and Ca. Next in abundance are Al, Fe, Pb and Zn. The total mass of particulates was about 20 µg kg^{-1} of air. Over the limited period of measurement there was a general increase in the concentrations in air during the winter compared with summer, as demonstrated in Fig. 1, for a number of the elements measured. This we attribute to the seasonal reduction in the vertical diffusion in the atmosphere; it is associated with the increased frequency of temperature inversions during the winter[26]. The rain concentration results combine the measurements of the soluble and insoluble contents. The soluble component is probably more available biologically and in future studies should be considered separately.

Certain derived parameters, "washout factor" W and "dry deposition velocity" V_g, are summarized in Table 1 together with the total deposition T and dry deposition D, all as mean monthly values during the year 1971. The magnitudes of total deposition generally follow those of the air concentrations: the proportion of dry deposition D/T is shown in Table 1. In the case of certain trace elements, Al, Sc, V and Fe, the dry deposition amounts on average to 15% or more of the total, although occasionally over shorter periods the dry deposition can account for more than half the total.

The washout factor W has been defined by Chamberlain[3] as

$$W = \frac{\text{concentration in rain (µg kg}^{-1}\text{)}}{\text{concentration in air (µg kg}^{-1}\text{)}}$$

and the manner in which this parameter averaged over 1971 varies according to element is shown in Fig. 2. Despite the variation over five orders of magnitude in air and rain concentrations the washout factors lie between 500 and 2,000 except for Na, Cl and Se. Within this range it is nevertheless possible to differentiate broadly between the trace elements, in that those having higher values of W are more easily washed out and therefore have higher concentrations in the atmosphere at the rain forming altitudes (~ 3 km), compared with ground level, than do the trace elements having lower values of W. It follows that high W is associated with a greater dispersion in altitude and therefore with a distant source whereas low W is associated with a more local source.

The dry deposition velocity V_g has been defined[3] as

$$V_g\ (\text{cm s}^{-1}) = \frac{\text{rate of dry deposition (µg cm}^{-2}\text{ s}^{-1}\text{)}}{\text{concentration in air (µg cm}^{-3}\text{)}}$$

The dry deposition velocities averaged over 1971 are displayed in a similar way in Fig. 3; most are seen to lie between 0.1 and 0.7 cm s^{-1}. The relationship between the mechanistic theory of dry deposition and our observations is not clear, especially when considering the effects of particle size, surface

Table 1 Annual Summary of Wraymires Results (January–December 1971)

			Parameter (annual mean)				
	Concentration in rain (µg l.$^{-1}$)	Concentration in air (ng kg^{-1})	Washout factor W	Total deposition/month T (µg cm^{-2})	Dry deposition/month D (µg cm^{-2})	D/T ratio	Dry deposition velocity V_g (cm s^{-1})
Na	2,300	800	2,900	27.5	1.35	0.05	0.53
Al	160	260	620	1.90	0.36	0.19	0.44
Cl	4,100	1,750	2,300	48.5	2.50	0.05	0.44
Ca	<1,100	520	<2,100	<13	0.95	0.06	0.57
Sc	0.042	0.059	710	0.0005	0.00019	0.38	1.01
V	4.1	8.0	510	0.049	0.0075	0.15	0.29
Cr	2.9	2.4	1,200	0.035	0.0022	0.06	0.29
Mn	8.1	10.6	760	0.096	0.008	0.08	0.24
Fe	200	230	890	2.35	0.41	0.17	0.57
Co	0.25	0.32	780	0.003	0.0003	0.10	0.29
Ni*	<6	5.5	<1,100	<0.07	<0.02	—	<1.1
Cu*	23	26	880	0.27	0.006	0.03	0.07
Zn	85	80	1,050	1.00	0.051	0.05	0.20
As	1.6	2.5	640	0.019	0.0019	0.10	0.24
Se*	0.34	0.90	380	0.004	0.00026	0.07	0.09
Br	17.0	27.1	620	0.20	0.017	0.09	0.20
Rb*	0.67	1.04	640	0.008	<0.00012	<0.15	<0.04
Cd*	<17.7	<3	—	<0.21	<0.02	<0.1	—
In*	<0.59	0.3	<2,000	<0.007	<0.0007	—	<0.73
Sb	1.8	1.6	1,150	0.021	0.00027	0.01	0.05
I	<2.5	<2.2	—	<0.03	<0.0004	—	—
Cs*	0.17	0.16	1,050	0.002	0.00012	0.06	0.23
La*	<0.3	<0.5	—	<0.004	<0.0005	<0.3	—
Ce*	0.42	0.30	1,400	0.005	<0.0005	<0.1	<0.52
W*	0.35	<0.86	—	<0.004	<0.0009	—	—
Au	0.01	<0.01	—	0.00011	<0.00001	—	—
Hg	<0.2	<0.17	—	<0.002	<0.0002	<0.1	—
Pb*	39	87	450	0.46	<0.05	<0.1	<0.18
Th*	0.12	0.13	920	0.001	0.0002	0.10	0.48

* Incomplete data.

Annual rainfall 142.7 cm.

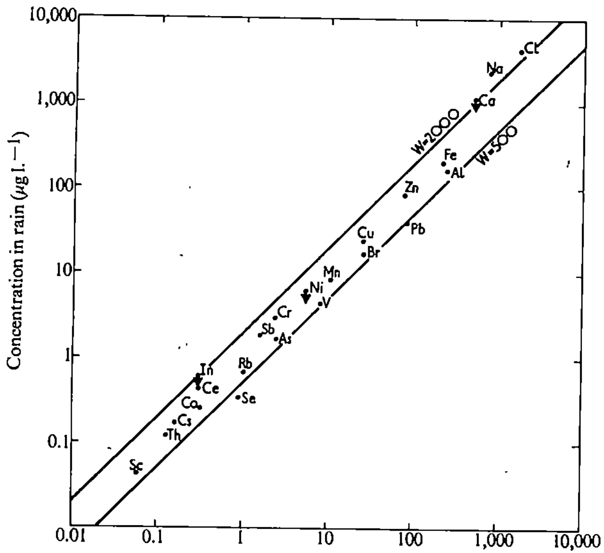

Fig. 2 Elemental concentrations in air and rain at Wraymires (1971).

roughness, wind velocity and other natural parameters. An important relationship in the present context is that between V_g and particle diameter d, and a semi-quantitative impression can be obtained from theory and data published by Chamberlain[27]. Broadly, the curve of V_g passes through a flat minimum in the region 10^{-1} μm$<d<1$ μm. Below this region V_g increases as gaseous diffusion becomes important: above, V_g becomes the terminal velocity due to gravitation at $d>10$ μm. The only quantitative scale, appropriate to the present experimental arrangement, that can be applied to V_g is derived from the measurements of radioactive fallout[28,29]. If $V_g=0.2$ cm s^{-1} for $d\sim 0.5$ μm then the range of values of d for the trace elements in Fig. 3 might lie between 0.1 μm and 10 μm; V_g increases with d. This is necessarily a simple interpretation and may be appropriate only to this method of collection. Thus it is unlikely that a natural aerosol can be represented by a single value of d, which must be characteristic of the property of the aerosol involved in the measurement of d.

Natural Origins of Trace Elements

It is now possible to review the possible origins, natural or artificial, of the trace elements measured at Wraymires by making use of the experimental observations, the derived parameters and other more general information. The summary values for V_g and W averaged over the year 1971 are combined in Fig. 4.

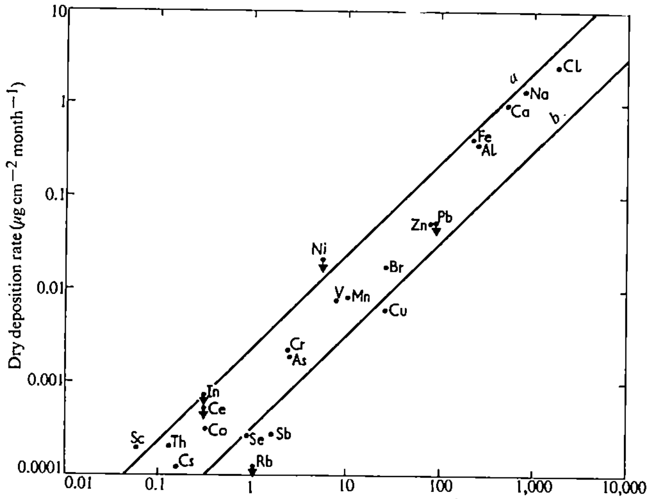

Fig. 3 Dry deposition and elemental concentrations in air at Wraymires (1971). *a*, $V_g=0.7$ cm s^{-1}; *b*, $V_g=0.1$ cm s^{-1}.

The ratio Cl/Na in air (2.2) is similar to but somewhat higher than the ratio in seawater (1.8): this similarity indicates a predominantly maritime origin for these two elements as does the correlation with wind direction (Briggs, private communication). Large values of washout factor W for Na and Cl suggest favourable conditions for washout; that is significant concentrations at the rainforming altitudes ($\sim$3 km) compared with ground level. The large particle sizes implied by the large values of the dry deposition velocities V_g are consistent with the hygroscopic nature of sodium chloride, thus further increasing the susceptibility to washout. The excess of Cl over the seawater proportion is probably industrial in origin as W is significantly lower than for Na. An increase in the ratio Cl/Na to >2 in the winter months had been noted previously in rainwater at Windermere by Gorham[30], who suggested that combustion of coal was responsible for the increase in Cl. All other trace elements except Br measured at Wraymires are present in seawater at such low concentrations relative to Na that a maritime origin is unlikely.

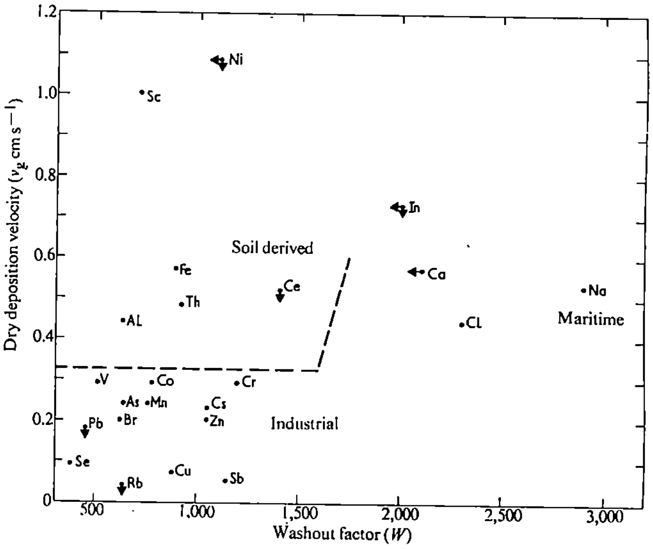

Fig. 4 Dry deposition velocity and washout factors at Wraymires (1971).

The other natural source of airborne trace elements is the soil, from which aerosols are raised by passing winds. The concentrations in air and rain may be compared with those measured in a sample of local soil (Grizedale series) and in soil generally, as listed by Bowen[31]. For convenience all concentrations are made relative to Sc, considered to be largely soil-derived, an assumption confirmed by high V_g and low W. Al, Mn (?), Fe, Rb, Ce and Th have approximately the same concentrations, relative to Sc, in air and soil; these elements, except Mn and Rb, lie in the sector of Fig. 4 that corresponds to high V_g, hence large particle size, and (except Ce) to low W, hence confinement to low altitudes. All other elements measured have concentrations in air relative to Sc greater or much greater than in soil, in particular Cl, Cu and Pb. A recent study by Rahn and Winchester[12] in Canada and Michigan suggested that most elements associated with larger aerosol particles, such as Al and Fe, had soil dust as their main source.

Other Sources of Particles

Those elements that are neither derived from the sea nor soil presumably have artificial origins. Generally, industrial processes involving combustion will yield small particles (<1 μm) formed by condensation, whereas natural particles formed by wind erosion and by grinding will be larger as noted above. Most of the trace elements that might be associated with artificial or industrial production lie conveniently in the sector of Fig. 4 below that of the soil derived elements. The trace elements of artificial origin have low V_g, corresponding probably to diameters <1 μm, and low to moderate W, implying sources ranging from local to more distant. Thus a likely origin for V is in fuel oil, and it is probable that the increase during winter[9] in the combustion of fuel oil for heating will enhance the seasonal variation noted previously. A fraction of Br may be maritime, on the basis of seawater concentrations relative to Na, but most is of industrial origin, either in fuel oil or as an ingredient of petrol. The ratio of concentrations in air Br/V$\sim$3.5 (Table 1) is similar to that found by Dams *et al.*[7] in Chicago. If the somewhat larger values of W for Cr, Sb, Cs and Zn are significantly different from those for the other artificial trace elements, then the former are likely to arise from the more distant sources. Iodine does not appear in Fig. 4 because the values of the derived parameters are indeterminate, but the occasional positive indications (>1 nano g kg^{-1}) of air could arise from the combustion of coal and oil[32,33]. Of the potentially toxic group of metals Pb, As, Se, Ni, Cd and Hg, only the first is present at Wraymires in notable concentrations in the air samples collected. The incomplete data for Pb are consistent with a low V_g and low W suggesting small particles formed in combustion locally. Lead is frequently attributed to motor vehicle exhausts, perhaps in association with Br. The ratio of concentrations in air Pb/Br$\sim$3.2 (Table 1) compares with the value of 2.6 in ethyl fluid reported by Lininger *et al.*[34].

Table 2 Comparison of Air Concentrations at Seven Sites in the UK, January–March, 1972

Element	Chilton, Berks	*Leiston, Suffolk	Lerwick, Shetland Is.	Plynlimon, Montgomery	†Styrrup, Notts	Trebanos, Glamorgan	Wraymires, Lancs
Na	650	1,620	3,430	400	920	840	790
Al	370	430	89	143	580	300	150
Cl	2,040	3,080	5840	920	4,180	2,130	1,750
Ca	550	<50	<50	<50	<50	<230	<200
Sc	0.10	0.089	0.019	0.032	0.15	0.17	0.05
V	22	19	3.5	5.4	26	20	17
Cr	3.6	14	1.4	1.0	12	11.1	2.7
Mn	21	38	4.3	8.2	49	20	15
Fe	380	549	102	160	785	502	271
Co	0.41	0.59	0.10	0.19	0.65	4.8	0.21
Ni	6.4	5.2	1.2	<5	9	54	<4.5
Cu	22	27	<1	18	55	40	22
Zn	194	327	64	117	415	302	132
As	6.5	8.5	2.5	2.0	19.3	7.5	5.4
Se	1.5	1.8	0.55	0.40	2.5	1.4	0.95
Br	48	34	18	11	102	46	28
Rb	<0.3	<0.3	<0.3	<0.3	<0.3	<1	<0.3
Cd	<4	<5	<4	<5	<5	<18	<4
In	<0.03	<0.03	<0.03	<0.03	<0.03	<0.1	<0.03
Sb	2.9	3.7	0.66	0.46	4.5	2.4	1.9
I	<0.1	<0.1	<0.1	<0.1	<0.1	<0.4	<0.4
Cs	0.30	0.51	0.09	0.11	0.51	0.27	0.20
La	<0.3	<0.3	<0.3	<0.3	<0.3	<1	<0.3
Ce	0.40	0.39	0.11	0.16	0.54	0.31	0.25
W	<0.3	<0.3	<0.3	<0.3	<0.3	<1	<0.3
Au	<0.003	<0.003	<0.003	<0.003	<0.003	<0.01	<0.003
Hg	0.15	<0.05	<0.07	0.05	0.09	0.24	0.13
Pb	98	103	43	35	380	208	139
Th	0.06	0.04	<0.03	<0.03	0.05	0.13	0.10

Concentrations are in ng kg^{-1} air.

* Leiston—data available for February and March only.

† Styrrup—data available for January and February only.

Of the trace elements that do not fall readily into the "maritime", "soil derived" and "industrial" categories of Fig. 4, the values of V_g and W for Ni and In are too uncertain for reasonable deduction. An anomalous position in Fig. 4 is occupied by Ca, which is unlikely to arise from a natural source in the quantities determined, although both V_g and W (upper limit) seem too high for artificial production by a combustion process.

Extensions of the Study

The concentrations measured in air at Wraymires have been compared with results obtained by other workers overseas[6,10,12,35]. Elements showing >10-fold increases relative to Wraymires in concentration in air from industrial regions in Japan[10] and the USA[6,35] are Mn, Fe, Zn, As, Sb, La, Ce, W and Hg. However, with the exception of Ce, the elemental concentrations in air at Wraymires exceed those reported for rural Canadian stations[12] which suggests that the Wraymires atmosphere is influenced by distant industrial activity.

The methods of sampling and analysis, the assessments of these methods, the measurements of trace elements in air, rain and dry deposition and a correlation with wind speed and direction have been described in detail elsewhere (AERE-R7134, in preparation). Finally, the programme of sampling and analysis at Wraymires has been extended to six other stations in the UK. To show how the results from Wraymires compare with levels from other non-urban sites, the concentrations of trace elements in air are listed in Table 2 for the first quarter of 1972.

We received help in the sampling arrangement and advice from the late F. J. H. Mackereth of the Freshwater Biological Association at Windermere.

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Wheat Germ Agglutinin blocks Mammalian Fertilization

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Wheat germ agglutinin specifically binds to the zona pellucida of hamster eggs and prevents sperm penetration and fertilization.

BEFORE fertilizing mammalian eggs, spermatozoa pass through a moderately thick transparent egg coat, the zona pellucida (ZP). There is evidence that the ZP is an important site for the species-specificity of fertilization[1-3] and the block to polyspermy[1,4,5]. The ZP has been characterized as glycoprotein or glycopeptide in nature[6-8], and it can be dissolved by proteolytic enzymes[6,9-13], oxidizing agents[6] and disulphide-reducing agents[6,13,14].

Characterization of ZP-Modifying Component

We found that hog pancreatic lipase (Sigma Chem.) dissolved the ZP of hamster eggs, but a crude wheat germ lipase preparation (Sigma Chem.) did not. Pretreatment with crude wheat germ lipase prevented dissolution of the

ZP by trypsin, pronase, papain, bromelain, ficin and also hog pancreatic lipase. The wheat germ lipase preparation increased the light-scattering properties of the outer surface of the ZP and prevented ZP penetration by spermatozoa.

Fractionation of the crude wheat germ lipase preparation yielded a "ZP-modifying", non-dialysable component that was heat-stable (30 min at 90° C). The molecular weight of this component was approximately 20,000–30,000 daltons, as shown by gel filtration chromatography using 'Sephadex' G-100, G-75 and G-50 and polyacrylamide gel electrophoresis. The size, heat-stability and the fact that the purified "ZP-modifying" component was capable of agglutinating rabbit erythrocytes suggested that it might be wheat germ agglutinin (WGA), a phytoagglutinin purified from a crude wheat germ lipase preparation[15] that specifically binds to oligosaccharides containing terminal (non-reducing) N-acetyl-D-glucosamine (NAGlcA) residues[16]. This was subsequently established by the following experiments: (*a*) molecular weight determination using gel chromatography and polyacrylamide gel electrophoresis; (*b*) agglutination properties (including inhibition by NAGlcA), and (*c*) immunological cross-reaction with WGA (purified by affinity chromatography)[17] in double diffusion tests with rabbit anti-WGA serum in the presence of NAGlcA. We therefore used affinity purified WGA in further studies.

Table 1 Effects of Wheat Germ Agglutinin on the Hamster Egg Zona Pellucida

Experiment	Treatment	WGA concentration (μg ml.$^{-1}$) 0	1	5	10	50	100	250	500
Light-scattering *	WGA †	—	—	—	+	+	+	+	+
	WGA→NAGlcA ‡	—	—	—	—	—	—	—	—
Resistance to trypsin §	WGA †	—	—	+	+	+	+	+	+
	WGA→NAGlcA ‡	—	—	—	+	+	+	+	+
Resistance to β-mercaptoethanol §	WGA †	—	—	—	—	+	+	+	+
	WGA→NAGlcA ‡	—	—	—	—	—	+	+	+
Sperm penetration ‖	WGA †	106/106	18/18	14/14	9/15	0/21	0/100	0/50	0/6
	WGA→NAGlcA ‡	82/82	16/16	15/15	25/26	11/30	0/19	0/29	0/7

* The outermost region of the zona pellucida scatters light strongly (+) or does not scatter light (−) under dark-field illumination.

† Eggs treated with various concentrations of wheat germ agglutinin for 30 min at 25° C and washed three times by transfer.

‡ Eggs treated similarly but were then incubated in a solution containing 0.1 M N-acetyl-D-glucosamine for 15 min.

§ Treatment with 0.01% trypsin or 0.1 M β-mercaptoethanol solution at 25° C. +, Failure to dissolve the entire zona pellucida within 30 min; —, zona pellucida completely dissolves within 5 min.

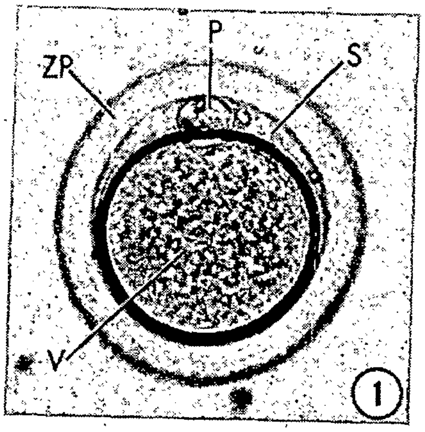
‖ Ratio of the number of eggs showing spermatozoa penetration of the zona pellucida within 2 h after *in vitro* insemination with capacitated spermatozoa to the total number of eggs used in three different experiments.

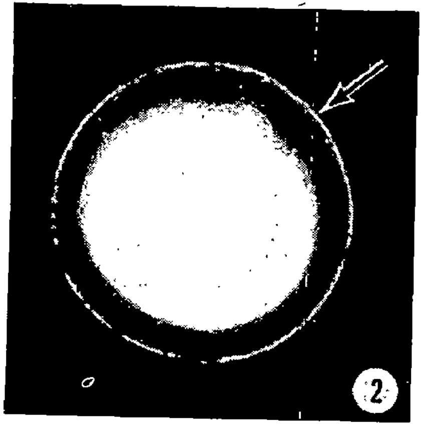
Binding of WGA to the Zona Pellucida

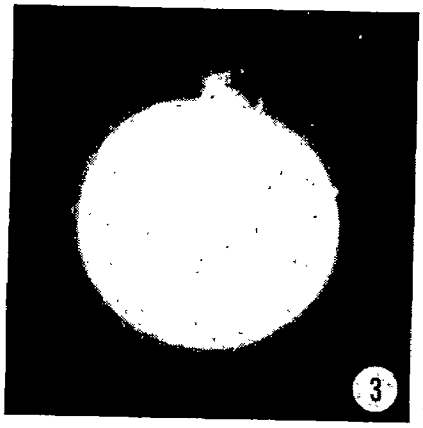
Unfertilized eggs were collected from adult female golden hamsters 16–17 h after injection of human chorionic gonadotropin[18]. Eggs were freed from cumulus cells by treatment for 15 min with Tyrode's solution containing 0.1% bovine testicular hyaluronidase (300 USPU mg^{-1}, Nutritional Biochem.). After thorough washing with Tyrode's solution, the eggs were incubated for 30 min at room temperature (about 25° C) in 0.9% NaCl–0.01 M Tris-HCl, *p*H 7.4, containing various amounts of purified WGA. After incubation with WGA, the eggs were rinsed three times for 5 min each in Tyrode's solution or isotonic 0.59% NaCl–0.1 M NAGlcA (WGA inhibitor), and some of the eggs were examined under dark-field illumination. Other eggs were exposed to a solution of 0.01% hog pancreatic trypsin (Trypsin 1–300, Nutritional Biochem.) or 0.1 M β-mercaptoethanol in 0.9% NaCl–0.01 M Tris-HCl (*p*H 7.4 at 25° C) to dissolve the ZP. The remainder of the eggs were tested for their fertilizability. One drop (50 μl.) of a suspension of cauda epididymal spermatozoa in Tyrode's solution was placed under mineral oil (Squibb Products Co.) in a watch glass and mixed with an equal volume of detoxified human serum[19]. After incubation for 4 h at 37° C the spermatozoa were considered to be capacitated, that is, capable of fertilizing hamster eggs. The eggs in approximately 20 μl. of Tyrode's solution were introduced into the suspension of capacitated spermatozoa, mixed and then incubated for 2 h at 37° C. Finally, the eggs were rinsed with Tyrode's solution and examined using phase-contrast microscopy for evidence of sperm penetration through the ZP and into the egg cytoplasm.

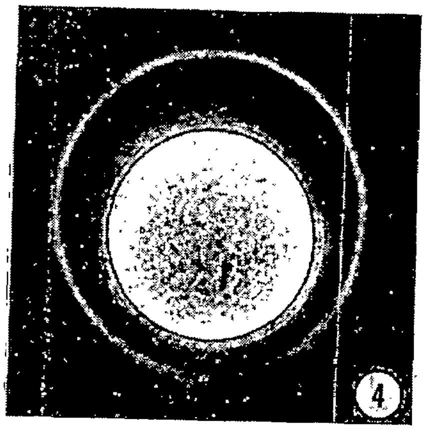
When hamster eggs are treated with WGA, it binds to the outer region of the ZP. WGA (10–500 μg ml.$^{-1}$) causes the outermost region of the ZP to scatter light strongly under dark-field illumination (Fig. 2; this can be compared with Fig. 1, an untreated egg, for the relative position of the ZP to the egg). The light-scattering properties of the ZP disappear after washing the WGA-treated eggs with an NAGlcA solution (Fig. 3 and Table 1). Other saccharides (sucrose, D-galactose, L-fucose and N-acetyl-D-galactosamine) fail to affect or reverse the ZP light-scattering properties caused by WGA. Further evidence that WGA binds to the outermost region of the ZP is that ferritin-conjugated WGA exclusively binds to this region, but not when NAGlcA is present (G. L. N. and R. Y., unpublished observation).

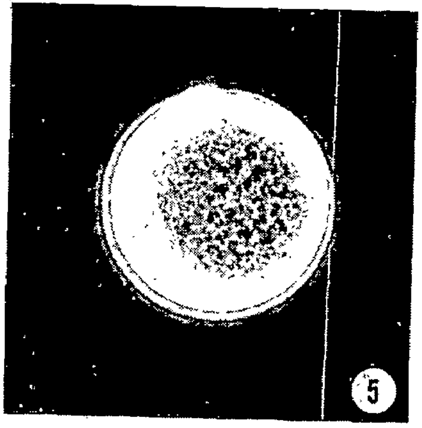
The outer region of the ZP is resistant to trypsin or β-mercaptoethanol dissolution after WGA treatment (Table 1). Concentrations of WGA greater than 5 μg ml.$^{-1}$ prevent trypsin dissolution of the outer region of the ZP when assayed 30 min after initiation of trypsin treatment (Fig. 4; compare with Fig. 5, an egg not treated with WGA). If the WGA concentration is 10 μg ml.$^{-1}$ or more, trypsin dissolution is prevented for at least 12 h. The trypsin resistance can be reversed by subsequent NAGlcA treatment when the eggs are preincubated with a low WGA concen-

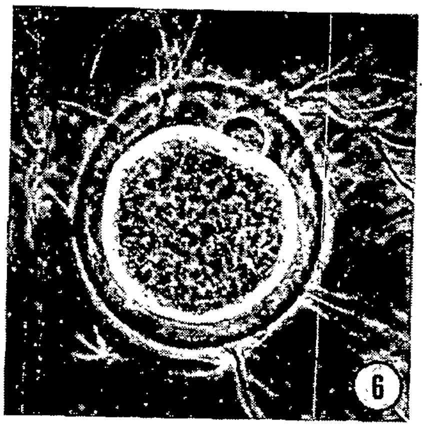


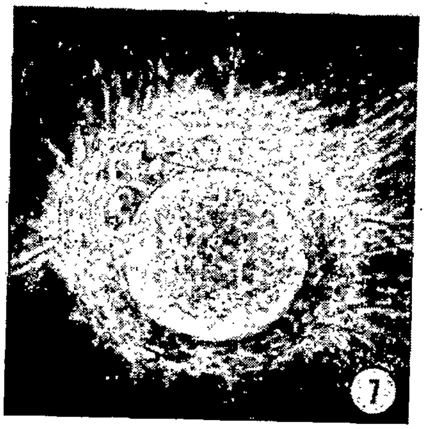


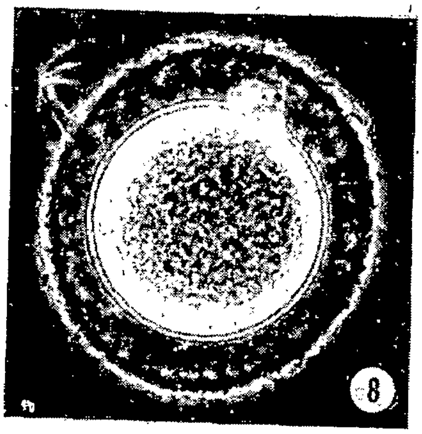












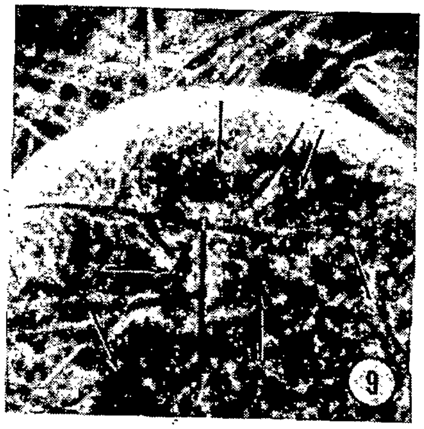


Fig. 1 Unfertilized hamster egg photographed with bright field light microscopy, showing the general structure of the egg. P, First polar body; S, perivitelline space; V, vitellus or egg proper; ZP, zona pellucida. ×380.

Fig. 2 Unfertilized egg treated for 30 min with wheat germ agglutinin (100 μg ml.$^{-1}$), showing strong light-scattering on the outer surface of the zona pellucida (arrow). Dark field, ×380.

Fig. 3 Unfertilized egg exposed to 0.1 M N-acetyl-D-glucosamine for 15 min after wheat germ agglutinin pretreatment (100 μg ml.$^{-1}$, 30 min). The light-scattering on the outer surface of the zona pellucida has disappeared. Dark field, ×380.

Fig. 4 An unfertilized egg pretreated for 30 min with wheat germ agglutinin (100 μg ml.$^{-1}$), and then exposed to a 0.01% trypsin solution for 30 min. The inner region of the zona pellucida has been dissolved by the action of trypsin, but the outer region of the zona pellucida remains undissolved. Phase-contrast, ×380.

Fig. 5 An unfertilized egg exposed to a 0.01% trypsin solution for 5 min without wheat germ agglutinin pretreatment, showing complete dissolution of the zona pellucida. Phase-contrast, ×380.

Fig. 6 After pretreatment with wheat germ agglutinin (250 μg ml.$^{-1}$, 30 min), an egg was inseminated with capacitated spermatozoa. Two hours later spermatozoa are colliding with the zona pellucida but fail to penetrate it. Phase-contrast, ×330.

Fig. 7 Following pretreatment with wheat germ agglutinin (50 μg ml.$^{-1}$, 30 min), an egg was inseminated with capacitated spermatozoa. Two hours later many spermatozoa are attached to the zona pellucida surface. Phase-contrast, ×330.

Fig. 8 Egg treated as in Fig. 7, but the spermatozoa (except for one at 10 o'clock) on the zona pellucida have been removed by agitation. There is no indication of sperm penetration into/through the zona pellucida. Phase-contrast, ×380.

Fig. 9 An egg (without wheat germ agglutinin pretreatment) was inseminated with capacitated spermatozoa. Two hours later the egg shows heavy sperm penetration. Arrows indicate swelling sperm heads within the egg cytoplasm. Phase-contrast, × 900.

tration (5 μg ml.$^{-1}$), but not at higher concentrations. If NAGlcA is present during the WGA treatment, the outer region of the ZP does not become resistant to trypsin dissolution. WGA also prevents β-mercaptoethanol from dissolving the outer region of the ZP at WGA incubation concentrations above 50 μg ml.$^{-1}$. This effect is also reversible at a low WGA incubation concentration (50 μg ml.$^{-1}$) (Table 1), and can be completely blocked by NAGlcA if it is present during the WGA incubation.

Egg Fertilization

Fertilization of eggs is blocked by WGA (Table 1). When eggs are exposed to WGA, washed and inseminated *in vitro* with capacitated spermatozoa, these fail to penetrate through the ZP. Spermatozoa are unable to make permanent attachment to the ZP of eggs treated with very high concentrations of WGA (>250 μg ml.$^{-1}$), although many spermatozoa constantly collide with the ZP surfaces (Fig. 6). When eggs are treated with lower WGA concentrations (50–100 μg ml.$^{-1}$), spermatozoa attach to the ZP surfaces (Fig. 7), but do not penetrate (Fig. 8). Untreated eggs, or eggs treated with very low concentrations of WGA (<5 μg ml.$^{-1}$), show heavy penetration of spermatozoa through the ZP (Fig. 9). WGA inhibition of fertilization is reversible with NAGlcA when the eggs are treated with low WGA concentrations (10–50 μg ml.$^{-1}$) (Table 1). If NAGlcA is present during the WGA incubation, fertilization is not prevented.

These findings are similar to those of Shivers *et al.*[20], where it was found that rabbit antibodies against whole hamster ovaries block hamster fertilization. They identified the immunoglobulins responsible for the inhibition of sperm penetration as anti-ZP antibodies. These antibodies produced a precipitation layer on the outer region of the hamster ZP and prevented trypsin dissolution of the ZP[21].

Our results indicate that WGA can block fertilization of hamster eggs by binding to oligosaccharides containing terminal NAGlcA in the outer region of the ZP. This region of the ZP may therefore be structurally different from the inner ZP region similar to the differences found between the inner and outer ZP regions of rabbit eggs[22]. Experiments with mechanically isolated hamster ZP indicate that the light-scattering optical properties associated with the specific binding of WGA are overwhelmingly localized in the outer ZP region and are not due to simple trapping or exclusion of WGA from the inner ZP region. (T. O., G. L. N., and R. Y., unpublished data). The loss of β-mercaptoethanol and protease susceptibility of the WGA-treated ZP could be due to steric masking of disulphide bonds and protease-sensitive polypeptide regions, or to allosteric changes in glycopeptide configurations that protect these sensitive bonds. A more likely possibility is that WGA does not prevent protease cleavage or disulphide reduction, but instead prevents the ZP matrix from dissolving by cross-linking oligosaccharide chains which are attached to adjacent polypeptides. If oligosaccharide cross-links are extensive, this could substitute an oligosaccharide-WGA ZP matrix for a disulphide-polypeptide matrix.

Treatment of hamster eggs with high concentrations of WGA (>250 μg ml.$^{-1}$) prevents attachment of spermatozoa to the ZP. At saturating WGA concentrations, sperm receptors on the ZP may be sterically or allosterically blocked. Another possibility is that sperm-borne proteases are necessary for attachment and penetration, and the activity of these enzymes is blocked by ZP-bound WGA, but this must be reconciled with the ZP resistance to protease dissolution following treatment at concentrations of WGA that allow some sperm penetration through the ZP (Table 1).

In the hamster the ZP becomes impenetrable by spermatozoa in less than 15 min after entry of the first spermatozoon into the egg cytoplasm[5]. This change in the properties of the ZP, the "zona reaction[4]", is thought to be induced by the cortical granule material which is released from the egg cortex as a result of fertilization[1,23]. Here it was found that WGA does not induce cortical granule breakdown; thus, the "zona reaction" is not involved in the prevention of sperm penetration by WGA. It is possible that the cortical granule material released after fertilization modifies the outer ZP region in a similar manner to WGA by steric masking of sperm receptor sites or by inducing allosteric changes in the glycopeptide matrix. As these changes are non-reversible, unlike the binding of WGA, it is probably more likely that the ZP is modified chemically by the cortical granule material.

The effect of WGA on hamster ZP does not appear to be a general property of phytoagglutinins, but instead is probably dependent on agglutinin saccharide specificity. Preliminary experiments with concanavalin A (specific for α-D-mannose-like residues)[24], *Ricinus communis* agglutinin (specific for β-D-galactose-like residues)[25] and *Dolichos biflorus* agglutinin (specific for N-acetyl-D-galactosamine-like residues)[26] indicate that concanavalin A does not entirely block hamster fertilization, but *R. communis* and *D. biflorus* agglutinins effectively block fertilization (T. O., G. L. N., and R. Y., unpublished observations). Concanavalin A sites are apparently more important on the egg surfaces of other species, such as the sea urchin *Paracentrotus lividus*, where it was found that concanavalin A (100 μg ml.$^{-1}$) effectively blocks fertilization and egg cleavage[27]. We are now studying the effects of different phytoagglutinins on fertilization and blastocyst implantation in the hamster and other mammalian species.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Properties of the Radio Continuum Emission from Interacting Galaxies

SEVERAL interacting galaxies have been observed recently in different programmes using the Westerbork Synthesis Radio Telescope at 21 cm wavelength (beamwidth 24 s × 24 s cosec δ). We give here a compilation of the data in order to examine the morphology, strength, and the frequency of occurrence of the radio emission from these interacting systems.

Table 1 Radio Emission from Interacting Galaxies

System	Other names	No. of members	Corrected total magnitude	Radio flux density 10^{-26} W m^{-2} Hz^{-1} at 1,415 MHz	Remarks
NGC 2444/45	VV117, Arp 143	2	11.7	0.020	Emission from the central HII complex in 2445
NGC 2798/99	Arp 283	2	11.7	0.072	Emission coextensive with 2798
VV150	Arp 322	4	13.7	0.025	Unresolved source in central galaxy
NGC 4038/39	VV245, Arp 244	2	10.2	0.212	Emission from dust patch between the galaxies
NGC 4438/35	VV188, Arp 120	2	9.5	0.060	Unresolved source in nucleus of 4438, and extended emission from dust patch nf
NGC 4485/90	VV30, Arp 269	2	9.3	0.900[5]	Emission coextensive with 4490
NGC 4676A/B	VV224, Arp 242	2	13.1	0.027	Unresolved source in nucleus of 4676A
NGC 5194/95	VV1, M51	2	8.0	1.6	Spiral emission from M51, and weak emission from 5195 (ref. 6)
Stephan's Quintet	VV288, Arp 319	5	11.7 —	0.027 0.040	Unresolved source in nucleus of 7319 Crescent shaped source between 7319 and 7318[12]

There are nine interacting galaxy systems in our sample and for five of these the optical photographs show luminous bridges or tails. Radio emission from these features could have been resolved from that of the other parts of these systems; however, in no case was any emission detected in the bridges or tails. The origin of the delicate structures is controversial, and there are two main points of view. It has been variously suggested that they are the result of repulsive forces[1], and that magnetic fields are important in producing their ordered, filamentary structure[2]. Recently, however, there have been successful attempts at explaining bridges and tails simply by gravitational tides during a close encounter of two galaxies[3,4]. Our failure to detect radio emission from these bridges and tails supports the latter interpretation.

To determine whether the radio emission from other parts of these interacting galaxies is unusually intense, we have compared our data with the results of Cameron's survey of normal galaxies at 408 MHz (ref. 7). In Fig. 1, we plot the flux densities against the corrected total apparent magnitude both for the interacting galaxies and for the normal galaxies. For the interacting galaxies, these magnitudes are computed from values given by de Vaucouleurs[8] or by Zwicky[9] using the same method described by Cameron[7]. In plotting the interacting galaxies we have used a 1,415 MHz flux density scale which is displaced from the 408 MHz scale by assuming that the flux densities vary as $(\text{frequency})^{-0.75}$. Normal galaxies at greater distances will extend the distribution in Fig. 1 along a 45° line towards the bottom left. It is clear that the interacting galaxies do not extend outside the region covered by normal galaxies; in particular, they do not extend above the rather well-defined upper boundary of the distribution. We therefore conclude that interacting galaxies in our sample do not emit significantly more powerful radio radiation than that of normal galaxies of similar optical magnitude. As a cautionary note, we mention that for the two systems which are common to our sample and that of Cameron, the higher angular resolution of our observations shows that unrelated nearby sources have caused Cameron to overestimate the flux densities of the systems themselves. Consideration of the number-flux density relation for radio sources leads us to believe that this confusion does not significantly affect the stronger sources in Cameron's sample, and that our conclusion is therefore still valid. A more precise statement must await the results of extensive high-resolution radio observations of galaxies now under way at Westerbork.

Purton and Wright[10] have recently published the results of their independent study of four interacting systems which were previously known to be radio sources (of which three are common to our sample). They combined their observations at 4.6 and 2.2 cm wavelength (beamwidth 3.8 arc min and 2.1 arc min respectively) with lower frequency data and concluded that the radio luminosities and spectra of the interacting systems are similar to those of normal galaxies.

The preceding comparisons show that the interacting galaxies

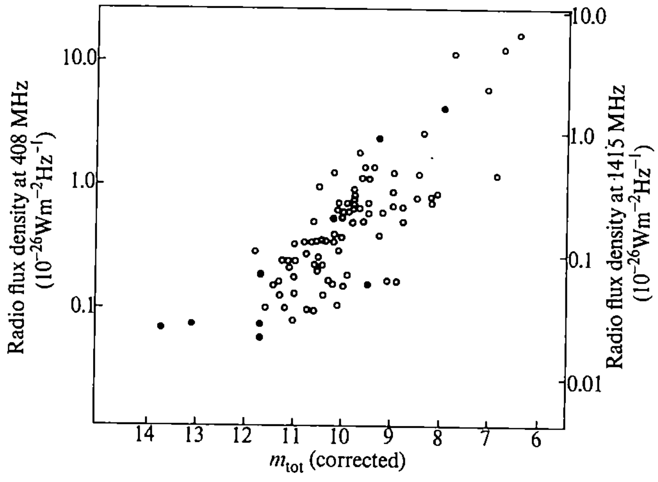

Fig. 1 Radio flux density *versus* total corrected apparent optical magnitude. ○, Detected normal galaxies; ●, detected members of interacting systems. The 1,415 MHz flux density scale is displaced from the 408 MHz flux density scale by assuming a spectral index of −0.75.

are not significantly stronger radio emitters than normal galaxies. We can further ask whether they are more frequent radio emitters. It is interesting that radio emission was detected in every interacting system observed; however, if we count the total number of galaxies in the systems we find nine detections out of twenty-one galaxies, omitting NGC 4485/90 because it was known from ref. 5. This number is not significantly higher than that found by Van der Kruit[11] (three out of ten) or by Cameron[7] (92 out of 264). But it is difficult to draw a firm conclusion from these data without including effects of sensitivity and distance; this is hardly warranted until more extensive high-resolution surveys of normal galaxies are available.

We conclude that on the basis of the data presently available, most of the radio emission from systems of interacting galaxies can be accounted for both in frequency and intensity by the emission expected from the constituent galaxies themselves. This is further supported by the observation that the radio morphology of these systems is often similar to that of normal galaxies—either from the nucleus or coextensive with the optical image of a member galaxy. There are three interesting exceptions to this morphology in our sample; in NGC 4038/39, NGC 4438/35, and Stephan's Quintet[12], the present high-resolution observations reveal an unusual form of radio emission which is not centred on a member galaxy nor on any of the optical bridges or tails. It seems likely that in these cases at least part of the radio emission is a direct result of the physical interaction between members of the system.

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Radio Sources identified with Stellar Objects using Precise Radio and Optical Positions

IT is difficult to establish the identification of a radio source with an object of stellar appearance and neutral colour. We show in this letter that such identifications can be made by comparing radio and optical positions of accuracy better than 1 arc sec.

Hoskins *et al.*[1] have produced a list of sources containing radio positions determined at 408 MHz together with the positions of nearby optical objects. The radio positions have an accuracy of about 5 arc sec r.m.s. The optical positions were obtained from the Palomar Sky Survey prints, using the Molonglo two coordinate measuring machine and a technique similar to that described by Hunstead[2]. Because of the radio errors the optical positions were quoted in ref. 1 to the nearest second of arc although their r.m.s. error is believed to be about 0.5 arc sec in each coordinate. The positions of all optical objects within about 45 arc sec of the radio position were measured and divided into two groups: those falling inside an error region whose limits were two standard errors from the radio position, and those outside this region. In order to estimate the background rate of occurrence of each class of object, randomly selected areas of the Sky Survey prints totalling approximately 385 (arc min)^2 were examined and all objects classified. As a result of these counts, an identification with either a blue stellar object (BSO) or a galaxy (g) fainter than 19 mag was claimed only for objects within the error region, but brighter galaxies were considered as possible identifications at displacements up to 20 arc sec. No identifications were claimed with stellar objects of neutral colour (St) because the number of such objects found within the error regions did not differ significantly from the chance expectation.

The interferometer of the Royal Radar Establishment (RRE) has been used to measure the positions of radio sources at 2,695 MHz with a typical accuracy of about 0.5 arc sec r.m.s. in each coordinate: these sources have radio angular extents less than about 10 arc sec. A first list of positions has been published[3] and other lists are in preparation. There are 11 sources in these RRE lists which are common to the sources of ref. 1.

The common sources are biased towards flat radio spectra because the sources of ref. 1 do not appear in the 4C catalogue[4] and are therefore generally weaker than 2 f.u. at 178 MHz, while the RRE sources are nearly all stronger than 0.4 f.u. at 2,695 MHz.

A comparison of the RRE positions with the positions of the optical objects noted in ref. 1 has led to some revision of the identifications in ref. 1. We give the revised identifications in Table 1: they are based on RRE accurate radio positions and Molonglo accurate optical positions. The description of the objects is taken from ref. 1. One of the 11 radio sources has a blank optical field: the remaining 10 are all identified with optical objects. Of the 8 identifications suggested in ref. 1, 6 are confirmed, including all 5 that were classified as BSO? or BSO. Two suggested galaxy identifications are not confirmed: the radio sources are now identified with a BSO? in one case and a stellar object in the other. In addition, two sources not previously identified have now been identified with stellar objects. The alterations occur chiefly because the more accurate radio measures make the position coincidences with stellar objects significant, whereas in ref. 1 stellar objects within the error regions could not be distinguished from chance associations.

The r.m.s. differences between radio and optical positions for the 9 stellar or possibly stellar identifications are 0.92 arc sec and 0.80 arc sec in right ascension and declination respectively. The mean differences, $+0.42\pm0.31$ and -0.18 ± 0.27 arc sec, are not significantly different from zero. The good agreement in position concerns the accuracy of the two sets of measurements, which were made completely independently. Following the definition in ref. 1, the error region for optical-radio position differences is an ellipse of semi-axes 1.8 and 1.6 arc sec. The counts quoted in ref. 1 show that the probability of finding a stellar object of neutral colour brighter than 20 mag in the combined error regions for the 11 sources one such region is only 1 in 50. Galaxies or BSOs brighter than 20 mag are even less frequent. These statistics give a high degree of confidence to the present identifications, whatever type of optical object is involved.

Ten sources out of the 11 have abnormal radio spectra

Table 1 Radio Source Positions and Optical-Radio Position Differences

Source (ref. 1)	RRE radio (1950.0) Right ascension			RRE radio (1950.0) Declination			Optical-radio Δα	Optical-radio Δα cos δ	Optical-radio Δδ	Identification Object		Notes
1200+04.5	12 h	00 min	48.18 s	04°	31′	02.4″	+0.07 s	+1.0″	−1.7″	19 mag	BSO?	2, 3
1355+01.0	13	55	20.44	01	01	08.0						4
1421+12.2	14	21	04.61	12	13	26.2	0.00	0.0	−0.4	18	St?	5, 6
1442+10.1	14	42	50.48	10	11	12.4	−0.07	−1.0	−0.6	18.5	St	7
1502+10.6	15	02	00.16	10	41	17.8	0.00	0.0	−0.3	18.5	BSO	2, 8
1555+00.1	15	55	17.68	00	06	43.1	+0.02	+0.3	−0.7	19	BSO?	5, 9
1616+06.3	16	16	36.52	06	20	13.8	+0.06	+0.9	+0.6	19	BSO	2, 5
1656+05.3	16	56	05.62	05	19	46.8	+0.03	+0.4	+0.2	17.5	St	10
1716+00.6	17	16	49.86	00	40	11.3	−0.20	−3.0	−0.4	20	g?	2
1743+17.3	17	43	22.27	17	21	08.5	−0.01	−0.1	+0.4	19.5	BSO	2, 11
1754+15.9	17	54	18.90	15	54	02.9	+0.16	+2.3	+0.9	18.5	BSO	2, 12

Symbols, as used in ref. 1.
g, Galaxy of unspecified type.
BSO, stellar image which is significantly brighter on the O ("blue") than on the E ("red") Sky Survey print.
St, Stellar image other than BSO.
? Indicates a doubt as to the nature of the object.

1. These sources appear also in other catalogues: for details see ref. 1.
2. Ref. 1 identification confirmed by RRE radio position.
3. The object may be a compact galaxy with a blue nucleus: it is stellar on the O plate and nebulous on the E plate. It lies in a faint cluster of galaxies.
4. Blank optical field.
5. RRE radio position from ref. 3, with right ascension reduced by 0.03 s to match AGK3 system.
6. St? lies in error region of ref. 1 but was not taken as an identification. Ref. 1 noted that the object is slightly blue and could be a BSO; re-examination of the Palomar Sky Survey confirmed that it is a BSO.
7. The present identification was first given by Véron[9,10] who took the object to be blue. Our re-examination of the Sky Survey makes it neutral in colour.
8. This source has been identified by Blake[6]. It is a quasar with a redshift of 0.57 (Burbidge and Strittmatter[8]).
9. Ref. 1 identification with 19.5 mag phase g ? lying in the error region not confirmed. BSO? lies outside the error region of ref. 1. The object may be a compact galaxy with a blue nucleus: it is stellar on the O plate and nebulous on the E plate. The present identification was first given by Véron[9] using an RRE radio position.
10. St lies in error region of ref. 1, but was not taken as an identification.
11. Another 19.5 mag BSO lies 12 arc sec from the radio position[1].
12. Two other 18.5 mag BSOs lie 17 and 25 arc sec from the radio position[1].

(peaked, flat, inverted or complex). This is inherent in the selection and is also confirmed by measurements over a range of frequencies (H. S. M. and D. G. H., in preparation). Only the source 1716+00.6 has a normal spectrum (spectral index −0.8) and this is the only source identified with a galaxy. It appears in the present sample only because it occurs in a region where the 4C survey is obscured. The optical-radio difference in right ascension of −3.0 arc sec is significant in terms of the r.m.s. differences given above, and suggests a real separation between the optical and radio centroids of this source.

Of the 10 sources with abnormal radio spectra, 1 has a blank optical field and 9 are identified with optical objects. The Palomar Sky Survey images of these 9 objects were re-examined to check the type of those considered uncertain in ref. 1. The results of this examination are given in the notes to Table 1: the only definite change is that 1421+12.2 is classified as a BSO rather than an St?. The two sources classified as BSO? may be galaxies, but this is uncertain. (Identification of 1555+00.1 is of interest because the radio source has been shown by very long baseline interferometry[5] to have most of its flux density in a component less than 0.0004 arc sec in extent: it has an inverted spectrum at low frequency possibly peaking between 5 and 10 GHz). The 10 sources thus comprise one blank field, 5 BSO, 2 stellar objects of neutral colour and 2 BSO? which may possibly be galaxies. The proportion of identifications with blue or neutral stellar objects (90% or possibly 70%) is much larger than the proportion found in samples of radio sources selected without regard to spectrum. Blake[6] and Fanaroff and Blake[7] have reported a similarly high identification rate with known or suspected quasars for sources with similar radio spectra to those discussed here.

The most interesting identifications are those of 1442+10.1 and 1656+05.3 with stellar objects of neutral colour. Confirmation of the nature of these objects would be highly desirable: they might, for instance, be quasars of high redshift.

The present work shows that stellar objects of neutral colour cannot be ignored as possible identifications with radio sources, and that radio and optical positions both accurate to better than 1 arc sec can produce such identifications. With combined radio and optical errors of about 5 arc sec, agreement in position is likely to be due to chance unless the radio spectrum is abnormal, in which case the probability of a genuine identification is greatly enhanced.

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Relativistic Behaviour of Circumnavigating Clocks

CONSIDERABLE interest has been aroused by Hafele's suggestion[1,2], subsequently supported by experiment[3], that caesium beam clocks, borne by commercial jets circumnavigating the Earth, may provide supporting evidence for the famous prediction of Einstein's theory of relativity that if one member of a set of twins departs from the Earth in a spacecraft and later returns to reunite with his sibling, he will be the younger of the two. Strictly speaking, this statement is valid only if the frame of reference in which the home-bound sibling remains at rest is an inertial frame, which is not true of a frame of reference attached to the (rotating) Earth. This fact was ordinarily disregarded because the relative velocities involved were supposed to be much larger than the velocity difference caused by this circumstance. But in the case of clocks employed by Hafele and Keating[3], this supposition is not true and the influence of Earth's rotation must be reckoned with.

In Hafele's calculation[1,2], a nonrotating frame of reference embedded in the Schwarzschild metric of the Earth played an intermediate role. Of course, the final result was expressed in terms of the ground speed of the flying clock. For flights confined to circular orbits in the equatorial plane, Hafele showed that

$$(\mathrm{d}\tau/\mathrm{d}\tau_0) \simeq 1 + gh/c^2 - (2\Omega Ru + u^2)/2c^2 \qquad (1)$$

where $g = GM/R^2 - \Omega^2 R$ and M, R and Ω are the mass, the radius and the angular velocity of the Earth. Equation (1) contains a directional effect which arises from the term linear in u (u positive for eastward flights, negative for westward) and is related to the fact that the speed u is measured in a rotating frame of reference. This seems to have been overlooked by Schlegel[4] when he suggested that the directional effect appearing in equation (1) may be erroneous. Here, I present a calculation, made directly in the rotating frame of reference, which not only vindicates Hafele's result but also generalizes it to more practical situations.

In an arbitrary frame of reference, the space-time metric is

$$\mathrm{d}s^2 = g_{ik}\,\mathrm{d}x^i\,\mathrm{d}x^k \qquad (2)$$

where $x^i \equiv (x^\alpha, ct)$; $\alpha = 1, 2, 3$. The metric tensor g_{ik} includes the effects of gravitation as well as of the noninertial nature of the frame of reference. The proper time of a standard clock is then given by[5]

$$\mathrm{d}\tau = \mathrm{d}t[-g_{44} - 2g_{\alpha 4}(u^\alpha/c) - g_{\alpha\beta}(u^\alpha u^\beta/c^2)]^{1/2} \qquad (3)$$

where $u^\alpha = (\mathrm{d}x^\alpha/\mathrm{d}t)$. For a clock at rest, equation (3) reduces to

$$\mathrm{d}\tau = \mathrm{d}t(-g_{44})^{1/2} \simeq \mathrm{d}t(1 + \Phi/c^2) \qquad (3a)$$

where Φ is the Newtonian potential at the position of the clock. In a Lorentz frame, this becomes

$$\mathrm{d}\tau = \mathrm{d}t(1 - u^2/c^2)^{1/2} \qquad (3b)$$

Now, if the underlying metric is of the Schwarzschild type (arising from the mass M of the Earth) and is viewed from a frame of reference K which rotates, with angular velocity Ω, with respect to the system of "fixed" stars, then the nonvanishing elements of the metric tensor, in the spherical coordinates (r, θ, φ), are given by[6]

$$\left.\begin{aligned} g_{11} &= \left(1 - \frac{2GM}{c^2 r}\right)^{-1}, g_{22} = r^2, g_{33} = r^2 \sin^2\theta \\ g_{44} &= \left(1 - \frac{2GM}{c^2 r} - \frac{\Omega^2 r^2 \sin^2\theta}{c^2}\right), g_{34} = g_{43} = -\frac{\Omega r^2 \sin^2\theta}{c} \end{aligned}\right\} \qquad (4)$$

Substituting (4) into (3), and for slow motions ($u^\alpha \ll c$) and weak fields ($\Phi \ll c^2$),

$$\mathrm{d}\tau \simeq \mathrm{d}t\left[1 - \left(\frac{GM}{c^2 r} + \frac{\Omega^2 r^2 \sin^2\theta}{2c^2}\right) - \left(\frac{2\Omega r^2 \sin^2\theta(\mathrm{d}\varphi/\mathrm{d}t) + u^2}{2c^2}\right)\right] \qquad (5)$$

In comparing the rates of two given clocks, the coordinate differential $\mathrm{d}t$ is eliminated.

Equation (5) contains two effects: the effect of altitude which, for $r = R + h(h \ll R)$, takes the form gh/c^2 where $g\{= GM/R^2 - \Omega^2 R \sin^2\theta\}$ is the "measured" value of the acceleration due to gravity at a place of colatitude θ; and the effect of motion of the clock which is directional, because of the occurrence of the product $\Omega(\mathrm{d}\varphi/\mathrm{d}t)$, and for $\theta = 90°$ reduces to the Hafele expression $-(2\Omega Ru + u^2)/2c^2$.

Equation (5) may be applied to a satellite-borne clock as well. I consider motion in a circular orbit, of radius R^*, inclined at an angle λ to the equatorial plane of the Earth. Measuring φ from the line of nodes, in frame K

$$\theta = \cos^{-1}(\sin\lambda \sin\alpha), \quad \varphi = \tan^{-1}(\cos\lambda \tan\alpha) - \Omega t$$

where angle α locates the satellite in its own plane of rotation: $\dot{\alpha} \equiv \omega = \sqrt{GM/R^{*3}}$. Equation (5) then gives

$$\mathrm{d}\tau^* \simeq \mathrm{d}t\,(1 - 3GM/2c^2 R^*) \qquad (6)$$

which is independent of λ and Ω, and depends only on R^*. In K_0 one would have

$$\mathrm{d}\tau^* \simeq \mathrm{d}t\,(1 + \Phi/c^2 - u^2/2c^2)$$

which, for $\Phi = -GM/R^*$ and $u^2 = \omega^2 R^{*2} = GM/R^*$, would again lead to equation (6).

Finally, comparing the satellite-borne clock with an Earth-bound clock (for which $\Phi = -GM/R$ and $u = 0$),

$$(\mathrm{d}\tau^*/\mathrm{d}\tau_E) \simeq 1 - (GM/2c^2)(3/R^* - 2/R) \qquad (7)$$

the Ω-term is now clearly negligible. Effects predicted by equation (7) are about 100 times larger than the ones encountered in the case of jet-borne clocks. Establishment of Skylab may subject these effects to a more decisive test.

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Large Window Spectracon

In the Spectracon[1] electronographic image tube, in the form now used for spectrographic recording, the image area is restricted to a rectangle 30 mm × 5 mm to enable a very thin (4 μm) mica Lenard window to be used which will support not only atmospheric pressure but also the pressure required to keep the electron-sensitive emulsion in intimate contact with the external mica surface when recording the image electrons.

Experience with this first type of tube has shown the high sensitivity of the device and high quality of the recorded images with excellent image definition, almost zero fog background, linear relationship of density with exposure and wide spectral range of sensitivity, thus making the tube very effective also for stellar photometry and the discrimination of faint objects against sky background. These possibilities were clearly shown by the work on stellar photometry by Walker[2]. This work also showed clearly the great advantage that would be gained if the effective window area could be substantially increased.

For some time Spectracons with mica windows 25 mm × 10 mm have been made and used successfully[3]. As the tube has unity electron image magnification, the photocathode must be of the same dimensions as the window and hence a photocathode plate 10 mm wide must be transferred into the tube and the transfer tube sealed off under vacuum without damaging the photocathode.

To make a tube with a substantially larger mica window, say, 25 mm × 20 mm, required also a photocathode of the same dimensions. Trials with mica windows 25 mm × 20 mm and ≈4 μm thick showed that these were surprisingly reliable and stood up to combined atmospheric pressure and also the application of emulsion-coated film many hundred times without fracture.

Thus the strength of the mica window seemed adequate and the outstanding problem was to provide the photocathode of necessary area. To insert a photocathode plate of 20 mm width through a glass transfer tube and seal it off proved very difficult. Hence, as a compromise, photocathodes were prepared on two glass plates 30 mm × 10 mm lying side-by-side in an activation tube. In this way, there was practically no discontinuity in the photocathode sensitivity along the edges adjacent to one another. These two plates were then transferred to the Spectracon envelope with a 25 mm × 20 mm mica window through a standard 11 mm transfer tube by the technique already described and mounted with the same sides in contact in the photocathode mounting frame. It was found to be very important to mount these plates with their photocathode surfaces accurately coplanar, otherwise electron-image distortion was serious.

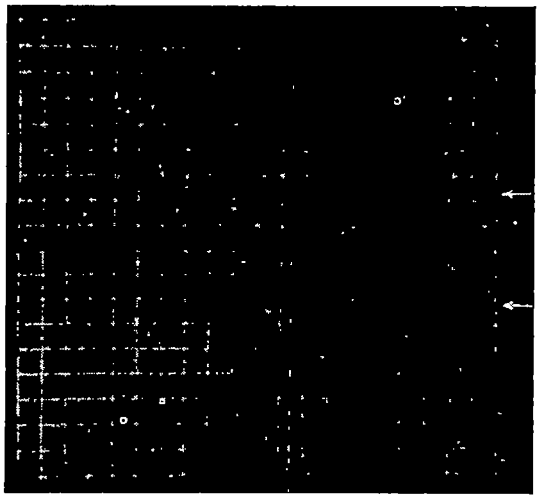

Fig. 1 Rectangular grid pattern 22 mm × 20 mm recorded by Spectracon. Arrows indicate effective width of window of "standard" Spectracon.

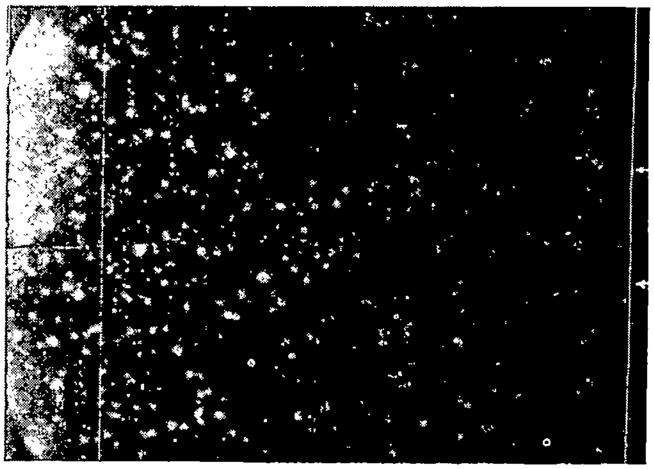

Fig. 2 Simulated star field picture reproduced by Spectracon (original size 25 × 20 mm²).

Only minor modifications to the tube, film applicator and focusing solenoid were necessary to make and operate this tube, and hence the device is convenient for use at the prime focus of a telescope. It has now been under test and in use for six months and has proved to be very reliable. The image quality over the effective image area of 25 mm × 20 mm is substantially identical with that of the standard tube over its window area of 25 mm × 5 mm.

Fig. 1 shows a reproduction of a grid pattern used to test the geometrical accuracy of the electron image, and it can be seen that, for an image tube, this is exceptionally accurate. In Fig. 2 is reproduced a recording of a simulated star field, such as might be recorded at the prime focus of a telescope, and it shows that the image quality is comparable with that of a standard tube. The discontinuity across the picture where the two photocathode plates join is clearly visible but is considered to be a small penalty to pay for the increase by a factor of more than four in the effective image area. A process for eliminating this is now being investigated.

It is not practicable to show in a reproduced photograph experimental evidence of the limiting resolution of this tube, but careful tests show that it is ≥ 70 l. p/mm over substantially the whole area shown in Figs. 1 and 2.

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Allende Meteorite Carbonaceous Phase: Intractable Nature and Scanning Electron Morphology

Meteorites, being solar nebula condensates[1], should carry information on the processes which led to formation of the planets. Within this context Green, Radcliffe and Heuer[2] studied 1 μm thick foils of the Allende C-3 chondrite by means of high voltage transmission electron microscopy (TEM). Its chondrules (small silicate spheres) showed features which suggested that they were older than the microcrystalline matrix which alone contained carbon. If the matrix crystallized directly from the circumsolar plasma as virgin planetary material[3] further study of its carbon phase would be of interest because little is known of the nature of the insoluble carbonaceous "polymers" of meteorites[4]. The Allende chondrite contains about 0.3% carbon of which 100 p.p.m., extractable by organic solvents, has been extensively studied[5]. The origin of this organic matter is an extremely controversial subject[6].

We have examined the ultrastructure of the Allende matrix by scanning electron microscopy (SEM) and isolated the carbonaceous phase for study by mass spectrometry and oxidative thermal analysis. SEM sample preparation consists of vacuum-deposition coating with conductive Au–Pd film a few angstroms thick. This was augmented by selectively etching the silicate matrix with gaseous fluorine generated in a Model IPC 1003B microwave plasma generator[7,8] supplied by International Plasma Corp., Hayward, California. SEM thus complements TEM by establishing the size range, three-dimensional appearance and shapes and types of particle arrays in the matrix. Energy-dispersive X-ray spectroscopy was used to determine the composition of μm-size areas for elements heavier than sodium. The Allende chondrite used in this study was specimen 818 from the Center for Meteorite Studies, Arizona State University at Tempe.

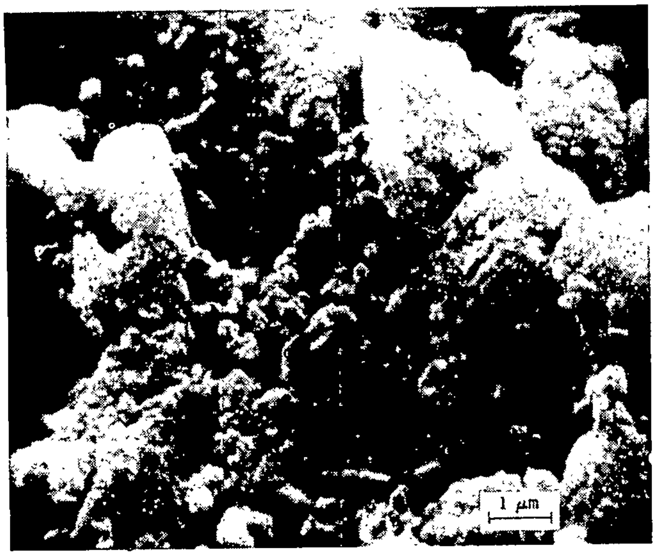

Fig. 1 Scanning electron micrograph of fresh Allende matrix fracture surface. Carbon aggregates and films which cover many areas in the central portion of the picture are seen by comparison with Fig. 2.

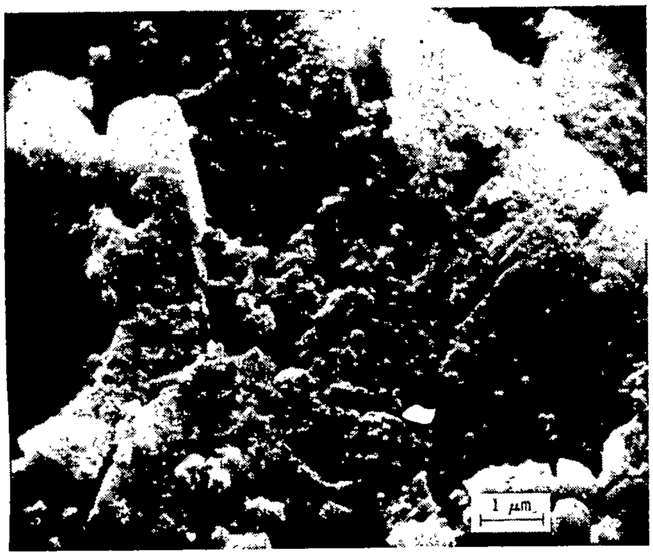

Fig. 2 Same area shown in Fig. 1 after exposure to plasma oxygen which has removed all carbon elements and consequently left prominent cracks exposed in several matrix crystals.

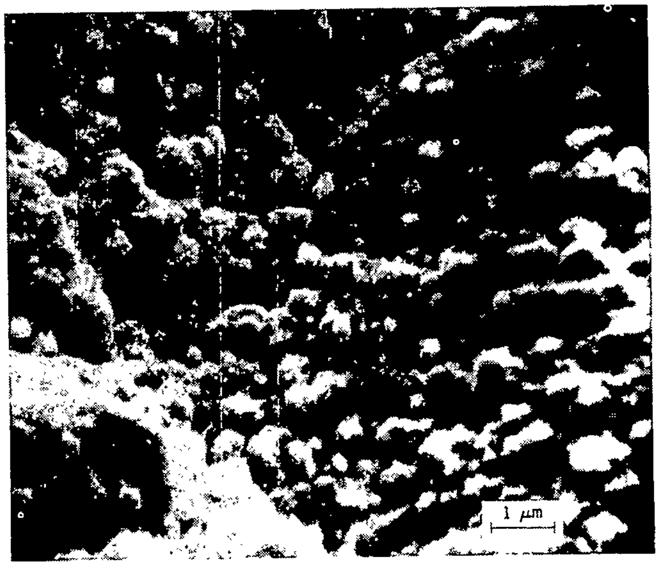

Fig. 3 A similar matrix fracture surface with numerous rounded microspherical carbon aggregates exposed by fluorine removal of the silicates.

An SEM view of an Allende matrix fracture surface (Fig. 1) contrasts sharply with that shown by TEM (ref. 2); it appears as a polymict breccia of randomly oriented forms some of which are anhedral. The grains are coated with a sodium–calcium rich glass and carbon occurs at the grain boundaries as irregular microspherical aggregates 1–3 μm in size, frequently with similar silicate forms. These carbonaceous areas give no response to energy-dispersed X-rays and they are quickly destroyed by plasma oxygen[9] (Fig. 2). Careful comparison of fresh and plasma oxygenated surfaces (Figs. 1 and 2, respectively) shows that the matrix also contains carbon as a surficial film about 0.1 μm thick which coats matrix grains but does not fill their surface interstices.

Exposure of a fracture surface to fluorine for an arbitrary period of 14 h (Fig. 3) exposes the carbon aggregates and clearly shows that they occur at former grain boundaries in roughly linear arrays. When the carbon is removed by exposure to plasma oxygen the fluorine has etched the silicate grains in such a way that they are also shown to be comprised of microspherical phases. These are seemingly identical morphologically to the subsolidus "liquid-crystalline" phases of feldspars described by Greer[10]. The carbonaceous aggregates vary from about 0.5 to 3 μm in size and are comprised of featureless spherical subunits about 0.05 to 0.2 μm in diameter. The "disordered graphite" area described by Green *et al.*[2] seems to be a cross-sectioned aggregate in which the spherical subunits appear as dark pinpoints.

The random (non-regularly packed) clustering of featureless carbon and silicate microspheres into irregular aggregates argues for their vapour phase growth in free space, with little interparticle interaction[11]. The mode of origin is not clear from morphology alone; they may have formed by *in situ* surface reactions on the matrix grains[12,13]. The size distribution and composition of the matrix also correspond to those postulated for interstellar dust[14,15], possibly trapped during nebular collapse.

Nearly identical carbon aggregates form from the liquidus mesophase of polycyclic aromatic hydrocarbons pyrolysed within very narrow temperature ranges at pressures of 1–30 kbar (refs. 16, 17). By analogy, the morphology of the Allende carbon and silicate microspherical aggregates suggests formation under high-pressure transient heating (and quenching), possibly as shock fronts displaced the asphalt threshold[18] within the unstable nebular cloud. These observations strongly

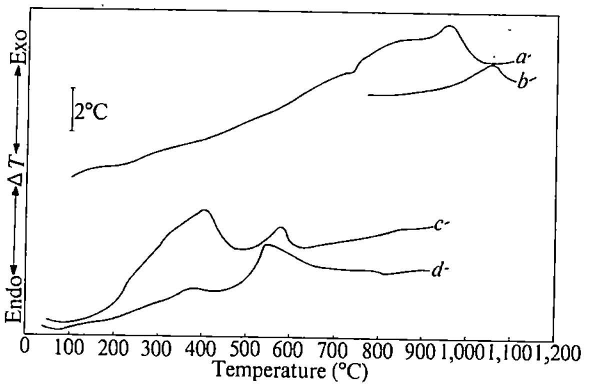

Fig. 4 Differential thermograms in an oxygen atmosphere: *a*, used Fischer-Tropsch iron catalyst; *b*, crystalline graphite, Essex Co., New York; *c*, Allende chondrite HF digest carbon phase, about 7.5% carbon; *d*, Allende chondrite ground to a particle size of about 100 μm.

support the theory of Arrhenius and Alfven[3] that primordial solar condensation took place by gas accretion.

Gaseous fluorine also causes sellaite (MgF$_2$) artefact aggregates to form on surfaces of peridot (olivine) (Mg,Fe)$_2$SiO$_4$ and magnesium silicate glasses but these are not confined to grain boundaries and are removed readily by boric or sulphuric acids. Carbon aggregates are never formed on minerals etched with the CF$_4$ microwave plasma decomposition products. The "temperature" of the plasma, about 40°–100° C, is insufficient to fluorinate carbon destructively[19]. The silicate microspherical aggregates also appeared when the matrix was etched with the "olivine-specific" etchant of Krishnaswami *et al.*[20]; they may be precipitates within grains, as noted by Green *et al.*[2].

An SEM examination of used Fischer–Tropsch catalyst showed its surface to be sparsely coated with carbonaceous aggregates nearly identical to those of the Allende meteorite. The sample, provided by Martin H. Studier, was Canyon Diablo siderite baked at 900° C and used to catalyse a "1 : 1 mixture of H$_2$ and CO for several days at 200° C"; its composition was C 0.66%, H 0.29% and N 0.0%. Studier, Hayatsu and Anders[21] have suggested that Fischer–Tropsch reactions may be sources of meteorite organic matter and this observation does not contradict that hypothesis.

A carbonaceous phase concentrate was prepared from the Allende stone by treatment with cold excess hydrofluoric acid (48%). The black partly gelatinous digest was taken up in dry acetone after being washed to neutrality with water; it was further dried by addition of 2,2-dimethoxy-propane and finally taken up in dry acetone alone. An aliquot determination of the final slurry showed 55.7% recovery of starting material. After crushing in an agate mortar to reduce undissolved chondrules the slurry was applied to a gradient column of acetone, chlorobenzene, chloroform, methyl iodide and bromoform[22]. The carbonaceous phase remained in the acetone from which it was recovered as a black powder with a composition of C 7.45%, H 1.36% and N 0.02%, or essentially as CH$_2$ "polymer". X-ray diffraction showed only sellaite (MgF$_2$) and an amorphous solid and its SEM appearance was identical to that of the microspherical aggregates exposed by fluorine on meteorite fracture surfaces.

The concentrate was insoluble in common organic solvents, in the equivolume mixture of nitrogen tetroxide–dimethylformamide which dissolves linear ionic polymers (and cellulose)[23] and in liquid ammonia at 25° C (ref. 24). Simon's reagent (Ag$_2$Cr$_2$O$_7$ in H$_2$SO$_4$) (ref. 25) attacked it at a rate 1.7 times less rapidly than graphite and it was unaffected by concentrated aqua regia at room temperature. Only traces of (principally) substituted benzenes were evolved when it was heated through 600° C in the solid inlet probe of an electron-impact mass spectrometer in complete agreement with the findings of Muenow, Steck and Margrave[26] who heated the whole chondrite through 1,500° C in a Knudsen cell within a mass spectrometer. Hayes and Biemann[27] reported similar results for the Murray and Holbrook chondrites. Spark source mass spectrometry[28] of the concentrate showed no cracking patterns for graphite[29], although numerous mass peaks for procedurally enhanced Mg and Ba fluorides and rare earths were present. The carbonaceous phase of the Allende chondrite is thus not a classical linear polymer nor graphitic.

Confirmation of its non-graphitic nature was provided by differential thermal analysis (DTA) in oxygen. DTA applied to coals and other kerogens[30] "ranks" them in terms of their peak exotherm temperatures which increase with diagenetically induced "fixed carbon" (graphite) content. By analogy, other complex systems can be similarly ranked and this has been done for the Allende, Mighei, Kainsaz and Grosnaja chondrites[4].

The present study was carried out at a very rapid nonlinear heating rate in flowing oxygen. A ballistic programme with a nearly linear rate of 80° C min^{-1} up to 600° C, which gradually decreased to 15° C min^{-1} at 1,000° C was obtained by applying full power to an 'R. L. Stone' 1,400° C platinum wound furnace which contained an 'R. L. Stone Series 11' open pan thermal head and a chromel–alumel ring thermocouple. A third connexion to the centre of the thermocouple permitted recording on the temperature axis of a DuPont 990 thermal analyser. Pure oxygen was swept through the system at 70 ml. min^{-1} to emphasize exothermic reactions. The DTA portion of this study, which included that of a number of other chondrites, will be discussed elsewhere.

The DTA results (Fig. 4) indicate that the Allende carbonaceous component is nongraphitic and that of the used F–T catalyst is similar to graphite. Reduced iron F–T catalysts are coated after use with hydrocarbon waxes and Hägg (Fe$_2$C) and other complex carbides[31] so that interpretation of this DTA data must await study. The rate of the F–T reaction which is, however, strongly pressure dependent would be vanishingly small in space except possibly under transient high pressure conditions (R. B. Anderson, personal communication). The two exotherms in the DTA data confirm the SEM observation that two forms of carbon are present in the meteorite. Comparison exotherms (°C) under these exact conditions are: (coals)—lignite 480, bituminous 555, anthracite 650, meta-anthracite 705 and graphite 800–1,060° C depending on degree of crystallinity. An attempt to isolate "Allende aggregates" from cellulase digests of filters flown through the debris cloud[32] was unsuccessful.

The morphology of the Allende matrix and its carbon phase revealed in this study suggests that the meteorite was formed by condensation from the gas phase in a complex series of events[1]. The nature of the non-graphitic carbonaceous phase is not clear although its intractable solvent properties and thermal stability suggest that it is not a polymer in the classical sense. Tamaru[33] has suggested that it may be an intercalation complex of amorphous carbon. Such sandwich complexes possess variable stoichiometry but those of graphite are regular, as for example K$_8$C. An investigation is in progress to determine the stoichiometry of the reaction product of the Allende carbonaceous phase and potassium in order to test this hypothesis.

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Saharan Glaciation Dated in North America

THE Lower Palaeozoic glaciation in the Sahara is rapidly becoming among the best known of fossil glaciations[1–3] but because rocks within and below the glacial sequence are poorly fossiliferous it has proved difficult to estimate the duration of glacial conditions. We suggest that the duration of the glacial episode is dated as extending from Lower Cambrian to Middle and perhaps Upper Ordovician by the occurrence in eastern North America of resedimented deposits indicating widespread simultaneous development of submarine canyons in response to glacio-eustatic lowering of sea level.

Eustatic sea level changes are chiefly responses to changes in the total volume of the mid-ocean ridge[4] and as such are controlled by spreading rate changes and changes in ridge length. These changes perhaps result from competition among mantle plumes[5]. Significant changes in sea level resulting from changes in ridge volume take place over periods of the order of 10^6 yr (ref. 4) and sedimentary processes governed by base level have little difficulty in adapting gradually to them. By contrast, glacially controlled eustatic changes take place over periods of less than 10^4 yr and produce sudden changes in base level. Daly[5] pointed out that glacial lowering of sea level greatly enhances submarine canyon activity and examples of canyon development related to the late Würm-Wisconsin low stand are widely reported (see for example ref. 7). We therefore suggest that a sudden onset of intense submarine canyon development recorded within a sedimentary sequence may be an indication that glaciation has started elsewhere. The criterion has to be applied cautiously because submarine canyons develop for a variety of reasons in tectonically active areas (for example in the Mediterranean[8]). Canyon deposits in the Late Permian of New Zealand are contemporaneous with a Late Permian glacial episode[9,10] but cannot be entirely dissociated from possible seafloor disturbance because they occur among thick marine deposits on the leading edge of a plate. The least ambiguous indications of glaciation beyond the ice-covered region are to be sought in miogeoclinal marine sequences with little contemporary tectonism. In contrast to tectonically controlled canyons glacio-eustatic canyons must start to develop at the same time all over the world. Final proof of the origin of a particular set of canyons comes by demonstrating both intercontemporaneity and contemporaneity with onset of glaciation. This has been achieved so far only for the Pleistocene and to some degree for the Permian. It should be possible to apply the same technique to the newly discovered Lower Palaeozoic glaciations because contemporary miogeoclinal wedges are widely reported.

The North American continental margin of the Proto-Atlantic Ocean during much of the Cambrian and Lower to Middle Ordovician was a carbonate shelf rather like the Sahul shelf north of Australia today[11]. Shelf limestones outcrop from Alabama to Newfoundland as well as in Greenland and Scotland over a minimum distance of 6,500 km (ref. 12). Because most coarse material resedimented from modern stable continental shelves passes down submarine canyons[13] we interpret major occurrences of coarse resedimented material down slope of the Cambro-Ordovician shelf break as evidence of submarine canyon activity and hence in this tectonically inactive environment of glacial events.

Comprehensive analysis of the age distribution of resedimented units must await refinement of Appalachian stratigraphy. As an example of the kind of analysis which

Table 1 Sedimentary Carbonate Breccias (XXX) Occurring at Ten Localities along 2,000 km of Strike in the Northern Appalachians

Ages	Frederick (Maryland)	Lancaster County (Pennsylvania)	Near Albany (N.Y.) in Taconic Klippe	Milton (N.W. Vermont)	Quebec (Levis P.Q.)	St. Jean Port-Joli (Gaspe P.Q.)	St. Fabien (Gaspe P.Q.)	Cow Head (Nfld.)	Humber Arm (Nfld.)	Hare Bay (Nfld.)
Middle Ordovician			XXX		XXX			XXX		
Lower Ordovician	XXX			XXX	XXX		XXX	XXX		
Upper Cambrian	XXX			XXX	XXX			XXX	XXX	XXX
Middle Cambrian		XXX		XXX	XXX			XXX	XXX	
Lower Cambrian		XXX		XXX		XXX				
Reference s	12	11	12	11	12	18	18	12	12	12
Page numbers	p. 187	p. 145	p. 85	p. 145	p. 117	p. 23	p. 35	p. 151	p. 151	p. 152

can be made at present we have set down (Table 1) the age distribution of coarse, resedimented, carbonate breccias at 10 localities in the Northern Appalachians. Episodes of resedimentation occurred from soon after the inception of the miogeocline in Lower Cambrian times to the changes in sedimentary polarity marking the development of tectonic lands to the south-east in Middle and Upper Ordovician times[14]. From this we infer that glacial conditions prevailed intermittently somewhere in the world from Lower Cambrian times to Upper Ordovician times. The western Sahara was polar throughout this time[15] and although most of the well preserved glacial deposits are Caradocian to latest Ordovician in age there is a record of Early Cambrian glacial deposits from Colomb Bechar[16] and there are widespread Eo-Cambrian glacial deposits in the western Sahara[17]. The incompleteness of the earlier record is not surprising because successive continental glaciations in the same area cannibalize sediments so that only the latest episode leaves a substantial record. Whether or not there was continuity from a widespread Late-Precambrian glacial event cannot be demonstrated on evidence from eastern North America because the miogeocline had not developed during the critical interval.

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Elemental Carbon in Marine Sediments: a Baseline for Burning

A RECORD of prehistoric and historic burning of carbonaceous materials may be found in the elemental carbon contents of the sedimentary columns. The widespread dissemination of such carbon as microcrystalline graphite is indicated by its presence in atmospheric dusts collected over the North Atlantic[1] and in ice nuclei collected from North Pacific airs[2]. Its submarine survival over geologic time periods, at least up to millions of years, is suggested by its occurrence in manganese nodules[3] and in sediments from the Sierra Leone Rise[1]. But a biologically mediated oxidation of elemental carbon in terrestrial soils has been proposed to explain the gradual disappearance of charcoals originating from forest fires[4]. The contributions of carbon from industrial activities are also visible and well documented (see, for example, ref. 5).

Prehistorically, the production of elemental carbon has been associated with the high temperature burning of plants and plant remains and in the formation of coal. Recent evidence[6] suggests that all ranks of coal from lignite to anthracite can be produced at temperatures below 200° C. There is an additional source from coal, oil or gas burning by human society. In energy production, depending upon the nature of the combustion process, it can achieve levels of around 5% in the residue[7]. Coal burning produces a variety of solids including magnetite, haematite, quartz and mullite. The latter mineral ($3\ Al_2O_3\ 2\ SiO_2$) is rather rare in crustal materials; it occurs in pelitic xenoliths in basic igneous rocks[8]. In coal ashes it varies between 0 and 16%. It may be a useful diagnostic tracer of coal burning and a search for the mineral in atmospheric dusts and in sediments might prove rewarding.

The dispersion of elemental carbon introduced to the atmosphere may be followed by its fallout patterns in the slowly depositing open ocean sediments. Further, in sediments of known accumulation rate, the carbon fluxes can be ascertained; carbon may also prove to be a useful tracer for other materials mobilized through the atmosphere as a result of fossil fuel combustion[9]. We have, therefore, attempted to provide a set of background values of natural (not induced by man) burning processes.

The carbon analysis is carried out by infrared spectroscopy and is based upon the development of a characteristic spectrum of elemental carbon produced during a long term grinding process[10]. Infrared bands at 1,720, 1,580 and 1,240 cm^{-1} are produced as a result of a high temperature and high pressure oxidation of the carbon surface during such grinding. Most elemental carbons, such as petroleum charcoal, lampblack, graphite, decolourizing carbon, and soot from oil or coal-fired furnaces, yield this spectrum. We chose petroleum charcoal as our standard substance because of its low ash content relative to the other carbons examined. We found that the absorbance of the 1,580 cm^{-1} band is directly proportional to the mass of carbon in the sample.

Table 1 The Elemental Carbon Contents of Pelagic Sediments

Sample	Depth interval (cm)	Depth (m)	Latitude	Longitude	Carbon content * (wt. %)
			Pacific		
LFGS 19G	0–10	2,799	57° 21′ N	150° 47′ W	0.090, 0.099
ANT 3 42P	0–5	2,386	56° 23′ N	171° 04′ E	0.098
Zts III 5G	4–15	4,714	45° 16′ N	158° 10′ E	0.051, 0.048
Zts III 4G	0–10	6,232	39° 30′ N	170° 51′ E	0.070
F/H 1a	0–10	5,700	39° 26′ N	148° 48′ W	0.060
Zts III 2G	0–10	5,773	37° 55′ N	150° 32′ E	0.082
Nova-A-1G	0–10	5,400	34° 23′ N	146° 02′ W	0.065
Scan 29 Pb	0–10	5,857	33° 16′ N	153° 44′ E	0.086
Scan 22P	0–10	3,862	32° 20′ N	159° 15′ E	0.024
Nova-A-2G	3–13	5,740	31° 35′ N	166° 34′ W	0.028
Zts VII 40G	0–15	5,050	30° 12′ N	143° 17′ W	0.070
Scan 21P	0–10	5,709	28° 59′ N	168° 55′ E	0.076
Nova-A-5G	3–13	5,894	25° 45′ N	175° 53′ E	0.037
LSD-H-101va	0–10	5,100	22° 08′ N	139° 00′ W	0.038
Scan P PGb	0–10	5,186	19° 56′ N	139° 52′ W	0.047
CRM 11G	0–15	5,820	16° 52′ N	156° 47′ E	0.032
7-Tow S K 1–5 FF	0–10	4,641	13° 46′ N	126° 07′ W	0.051, 0.049
Wah 6FF-2	0–10	4,787	6° 08′ N	152° 38′ W	0.015
Amph 133G	0–10	4,149	3° 32′ S	141° 26′ W	0.0047
Scan 78P	0–10	4,231	12° 15′ S	134° 19′ W	0.0056, 0.0055
Nova H 20G	0–10	3,063	12° 53′ S	176° 39′ E	0.0022
Scan 80G	0–10	4,697	24° 53′ S	143° 27′ W	0.0023
Nova-A-48G	0–13	2,220	28° 12′ S	158° 13′ E	0.00090
Msn 111G	0–15	5,230	40° 37′ S	164° 08′ W	0.027, 0.029
			Atlantic		
Zeph-I-22G	0–12	5,601	25° 05′ N	34° 13′ W	0.029
Zeph-I-23G	0–10	5,209	26° 14′ N	26° 27′ W	0.020
LSD-A-216V	0–10	2,820	3° 18′ N	31° 03′ W	0.019

* Duplicate values were obtained through analyses of the same isolate. The values are indicative of the precision of the method.

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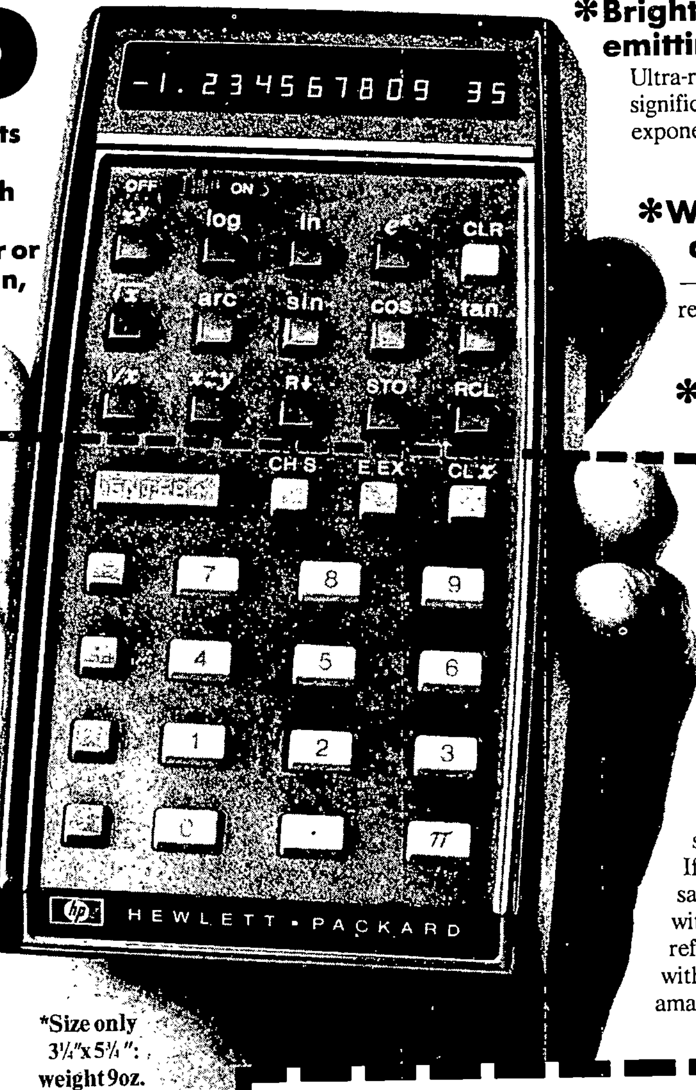

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A basic peroxide treatment of the gross sediments was sufficient to destroy a substantial portion of the organic matter without attacking the elemental carbon. This is a particularly important step because the spectra of some humic acids[11] are similar to that developed for carbon. Full details of our technique will be published later.

There is a marked increase in the carbon concentrations of pelagic sediments going from the southern equatorial regions northward (Table 1, Fig. 1). Clearly, normalizing the data to a time parameter (such as rates of accumulation) would be more reasonable. Because the more northerly deposits are more rapidly accumulating than their southern counterparts[12] the latitudinal differences in carbon accumulation per unit time would be even more dramatic. The carbon contents of the few Atlantic sediments analysed fit the general latitudinal dependence pattern of their Pacific counterparts. Because the rates of deposition of both groups are similar[12], this suggests that the same processes may be operative in bringing the carbon to the marine environment.

The most likely source of the carbon in these deposits (we have integrated over about the upper 15 cm of sediment, the past 100 m.y.; the top 0.5 cm, corresponding to the past 5,000 yr, was not included) is the debris produced in forest fires. Graphite may form during the thermal metamorphism of sedimentary rocks. But the observed latitudinal variations of carbon do not relate to the distributions of such materials and we did not pursue this possible source of carbon further. In Fig. 1 we have plotted the extent of four types of forest: conifer, non-coniferous temperate, Mediterranean, and tropical. If the burning hypothesis is correct, the primary contributors of carbon to the prehistoric sedimentary record are most probably the first three types of forests[13].

There is in general a latitudinal zonation of forest types about the Earth's surface (Fig. 1). The forests are distinguished by the type and extent of their vegetation which in turn reflects differences in soil, climate, elevation and past land use. At higher latitudes, before the ice sheets are approached, the tundra is covered by mosses and lichens with only occasional small trees. Cool coniferous forests belt the Scandinavian countries, across Russia to Siberia and continue over much of Northern Canada. Their trees consist largely of spruce, pine, fir, hemlock and cedar with some birch and willow. Southward, they blend into the temperate mixed forests of the eastern United States, the British Isles, central Europe and eastern Asia.

The tropical forests span the near equatorial regions. In the Amazon basin, western and west-central Africa and in south-eastern Asia are high concentrations of these forests. The combustion of tropical forest organic matter is through low temperature biologically mediated processes without the production of carbon. In contrast to these rain forests are the drier open woodlands or savannas, which contain primarily grasses and only small numbers of trees.

The winds which can move the debris of high temperature burning from the continents to the ocean environment are zonal. The three chief systems in the lower atmosphere are the easterly trades of the equatorial regions which blow from east to west, the westerlies of the mid-latitudes, much more intense at higher elevations and more variable, and the polar easterlies of relatively low intensity and high variability. Particles injected at one latitude will normally travel along it with spreading to the north and south due to the meanderings of the flow patterns. The principal contributions to atmospheric dusts are from the arid regions of the world; maximum burdens, as seen in their deposition to the marine sediments, occur at around 20–30° N and 30–40° S (ref. 14). Their transport is in the prevailing westerlies which most probably are responsible for the dispersion of much of the carbon produced in forest fires.

The relative production of carbon particles by forest fire burning and by fossil fuel combustion may be estimated on the following basis. The US production of particulates from the combustion of fossil fuels from stationary sources has been estimated as 6 mtons yr^{-1} (L. J. Shannon *et al.*, at 2nd International Clean Air Congress, Washington, 1970). A value for both stationary and moving sources of 10 mtons yr^{-1} has been quoted[15]. We use the lower figure, multiplied by a factor of 3 to extrapolate it to a global value, to estimate conservatively the introduction of carbon to the environment. Further, we assume that 1% of these particulates is elemental carbon, that its disposition is uniform about the northern hemisphere, and that it is not degraded in the atmosphere. On such a basis there would be an annual fallout on land and sea of 0.07 μg cm^{-2} of fossil-fuel generated carbon (a total of 0.18 mton).

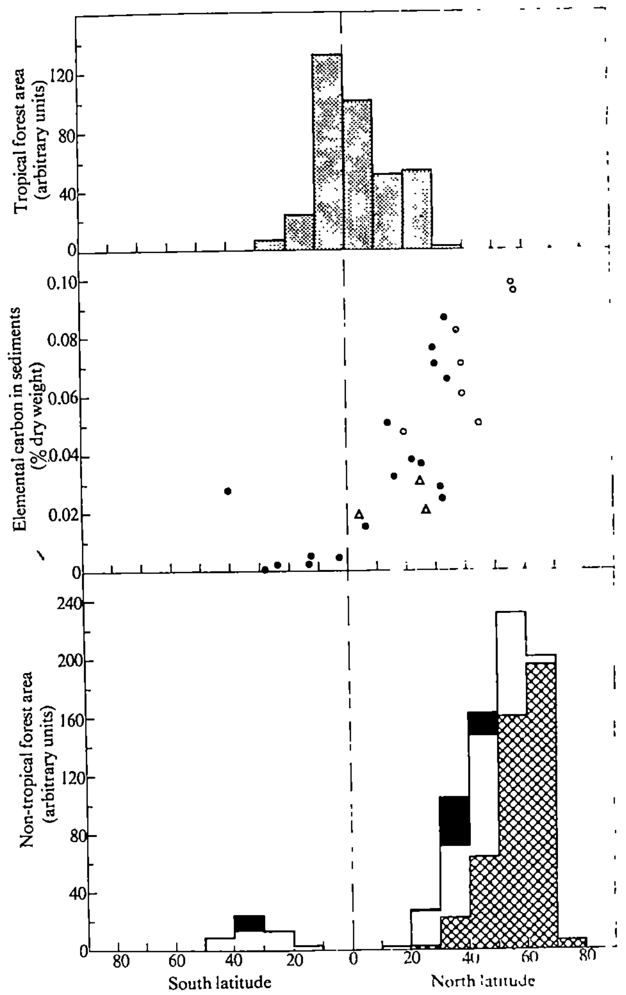

Fig. 1 The elemental carbon concentrations in Pacific deep-sea sediments as a function of latitude with the corresponding areal extents of forests[19]. In the lower histogram, the hatched areas represent conifer forests, the unshaded areas the non-coniferous temperate forests, and the black areas the Mediterranean forests. ●, Pacific; △, Atlantic.

Robinson and Robbins[16] make a rough assessment of the contributions of forest fire particulates to the total atmospheric aerosol burden. Again, these particulates are not totally carbon. The US has an annual forest fire area of 4.5 × 10^6 acre. This expanse is taken to represent 25% of the global forest fire area, 18 × 10^6 acre. The average amount of fuel burnt per acre is assumed to be 18 ton or 90% of the wood growing in forested areas. The particulate emission for such burning is estimated to be 17 pound per ton giving, as a total global emission, 3 × 10^6 ton annually. If 10% of this is carbon (0.3 mton yr^{-1} or 0.12 μg cm^{-2} of the Earth's surface, if emissions are assumed to be confined to the northern hemisphere), the forest fires and energy production are now contributing comparable amounts of carbon.

Other estimates of the production of these forest fire particles cited by Robinson and Robbins range from 27 mton yr^{-1} for the US alone with an addition of 17 mton yr^{-1} from slash burning and forest litter control operations, to a global particulate production of 150 mton yr^{-1}. This difference is not unexpected when the difficulties in dealing with such poorly defined numbers are taken into account.

The estimated elemental carbon emission from forest fires, 0.12 $\mu g\ cm^{-2}\ yr^{-1}$, seems to be in reasonable accord with the amounts which we have found in the North Pacific sediments. The rate of sedimentation for these deposits can be taken as 1 mm per thousand years[12]. With an average carbon content of 0.05% (Fig. 1; Table 1), and a density of 2 $g\ cm^{-3}$, the rate of accumulation of carbon is 0.1 $\mu g\ cm^{-2}\ yr^{-1}$.

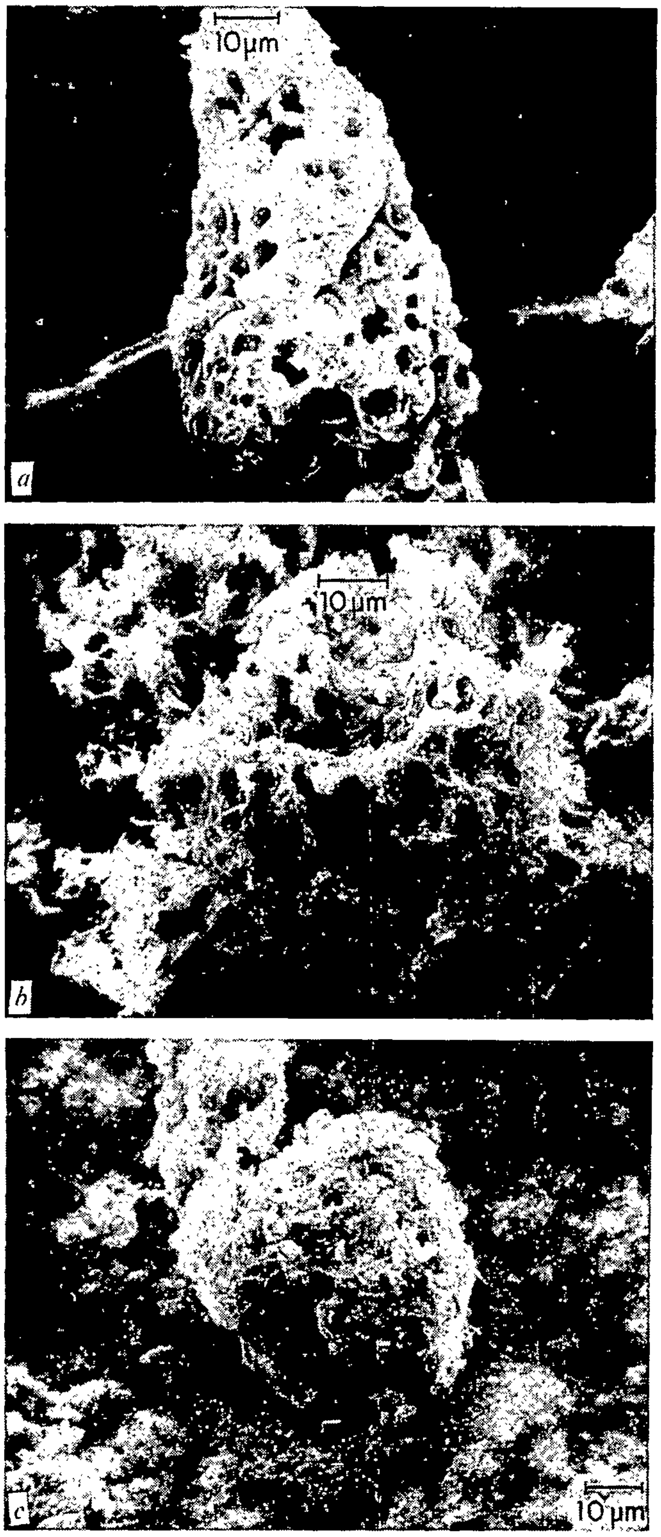

Fig. 2 *a*, Carbon particle isolated from forest fire particulates, San Diego County, Sample 56P; *b*, carbon particle from the chimney of a wood burning domestic fireplace; *c*, carbon particle isolated from Zts 40G.

Additional evidence that the carbon in these marine sediments has an origin in forest fires derives from scanning electron micrographs of carbon separates from flyash-containing sediments and atmospheric particulate matter collected downwind from a forest fire (Fig. 2). The forest fire occurred in the Julian–Poway–Ramona area, east of San Diego, on October 30, 1967 and the carbon particles were isolated from the bulk of the material by an HF-HCl treatment. The morphology of such particles is similar to those extracted from marine sediments. The larger carbon particles (diameter >20 μm) associated with forest fires and other wood burning (Fig. 2*a* and *b*) retain a morphology seemingly fashioned by the cellular structure of the wood[18].

The carbon particles in the deep sea sediments had diameters usually no more than several microns. Because of their small size these particles did not show any cellular features of wood. Occasionally larger particles were encountered (Fig. 2*c*) and bore a striking resemblance to particles produced in wood burning. Scanning electron microscopic studies on the larger carbon isolates from the sedimentary column seem promising to complement and to extend palaeopalynological investigations concerned with the extent and types of forests in past geological times.

Such size distributions are similar to those of atmospheric particulates of continental origin collected over the ocean[20], and support our aeolian transport thesis for the carbon particles.

We have made the implicit assumption that the extent of present day forests has persisted hundreds of thousands of years into the past (exclusive of glacial periods). Future work with the carbon contents of deep-sea sediments may reveal the validity of this concept. This work was supported by an EPA grant. D. M. S. is on leave from Hope College, and acknowledges an NSF fellowship.

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Man-made Objects on the Surface of the Central North Pacific Ocean

In August 1972, on the Scripps Institution of Oceanography's expedition C'BOG I in the Central North Pacific, there was a rare combination of clear warm weather and calm seas which tempted the scientific personnel to spend their leisure time on the bow of the ship. From this vantage point it was obvious that the sea surface is littered with a startling array of man-made objects, even 600 miles from the nearest major civilization (Hawaii) and outside the major shipping lanes.

A junk log was established and maintained (not continuously) for four days, during which time the ship travelled from 34° 29′ N, 145° 36′ W to 35° 00′ N, 155° 00′ W, and then south to 31° 00′ N, 155° 00′ W. Record was kept of the duration of watch, ship's speed and viewing conditions, and an effort was made to categorize each object, even though exact identification was often uncertain.

The results of this log are presented in Table 1. During 8.2 viewing hours during which time the ship travelled 156 km, and in approximately 12.5 km^2, a total of 53 man-made objects was recorded. Twelve of these were glass fishing floats, approximately 5 to 14 inches in diameter, which may claim some historic or aesthetic place on the sea surface. The remaining 41 objects were encountered with an average frequency of one every 12 minutes. At least two-thirds of these were plastic.

Succumbing to the temptation to extrapolate from our sample of six plastic bottles, we have calculated an average concentration of 0.5 bottle km^{-2} (95% confidence interval, assuming a Poisson distribution: 0.2–1.0 bottle km^{-2}) and a total of 35.4 million plastic bottles (14.2×10^6–70.8×10^6) currently adrift in the North Pacific Ocean (as well as 5.9 million red rubber sandals). A more conservative estimate may be derived from the observed ratio of plastic bottles to fishing floats, of which there are an estimated ten million afloat in the Pacific Ocean[1]. Our ratio predicts five million plastic bottles.

Table 1 Tentative Identification of Man-made Objects adrift in the Central North Pacific Ocean

Plastic		Glass		Miscellaneous	
Bottles	6	Fishing floats	12	Rope	1
Fragments	22	Bottles	4	Old balloon	1
Total	28	Total	16	Finished wood	1
				Shoebrush	1
				Rubber sandal (red)	1
				Paper items	3
				Coffee can	1
				Total	9

On two of the plastic bottles, algal growth was evident. A third was covered with gooseneck barnacles. Floating plastic, like a glass fishing float, provides a long-lived substrate for transport of sessile animal species as well as algal and bacterial growth; whether the increased availability of such "micro-arks" might alter distributional patterns or attract local concentrations of associated pelagic organisms is an open question.

In the growing concern over global pollution, the accumulation of plastic products has received little attention. Widespread concentrations of plastic pellets have been reported in the Sargasso Sea[2]. Although plastic objects may directly injure wildlife[3], the inert nature of plastic means that it is unlikely to enter the food chain and threaten human welfare. As a pollutant, its effect is chiefly aesthetic, which is difficult to evaluate and easy to ignore. We find it alarming that "disposable" items now litter even the most remote surfaces of the oceans.

The production of plastics has evolved rapidly during the past twenty years—annual production of plastic bottles now exceeds 5×10^9. The development of degradable plastics may bring some relief[4], but unless we find adequate means of disposing of our plastic products soon, we can anticipate that the "Wynkin, Blynkin and Nod" of our children will set sail into a plastic sea, accompanied by all the "no-deposit—no-return" products of our technology.

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Induced Nucleophilic Substitution in Benzo[a]pyrene

Cavalieri and Calvin have proposed[1,2] that the carcinogenic action of benzo[a]pyrene (BaP) may arise from aryl hydroxylase induced binding to nucleophilic cellular components. Their theory proposes that attack by electrophilic oxygen, produced in the hydroxylase system, occurs at the 6 position of the hydrocarbon to give a carbonium ion, localized primarily at the 1 and 3 positions, which can undergo attack with nucleophilic cellular components. Alternatively, initial attack could occur at 1 or 3, followed by nucleophilic reaction at 6.

Some evidence for the theory has been obtained by using iodonium ion as a model for the hydroxylase system. Benzo[a]pyrene and iodine dipyridine nitrate react to give either the 6-iodo or 6-pyridinium derivative or a mixture depending upon reaction conditions. Effects of solvent, concentrations and ratios of reactants were investigated and are summarized in Table 1. Equimolar quantities of the reagents react within 10 min in chloroform to give 6-iodo-benzo[a]pyrene in nearly quantitative yield. All other reactions listed required up to 24 h to reach completion. Formation of the pyridinium derivative requires a 2 : 1 molar ratio of iodonium reagent to BaP.

Table 1 Effect of Reaction Variables on Product Formation

Concentration of BaP	Molar ratios py/BaP*	Molar ratios (py-I-py)†/BaP	Solvent	Yield, % I-BaP	Yield, % py-BaP
		1	$CHCl_3$	99	Trace
		1	MeOH	95	
		1	DMF	95	
			Pyridine	No reaction	
1 mg ml.$^{-1}$	32	2	1% py/$CHCl_3$	50†	50†
0.5 mg ml.$^{-1}$	64	2	1% py/$CHCl_3$		95
5 mg ml.$^{-1}$	30	2	5% py/$CHCl_3$		95
5 mg ml.$^{-1}$	30	1	5% py/$CHCl_3$		50
1 mg ml.$^{-1}$		2	CH_3CN		10

* Added pyridine.
† Approximate yields.

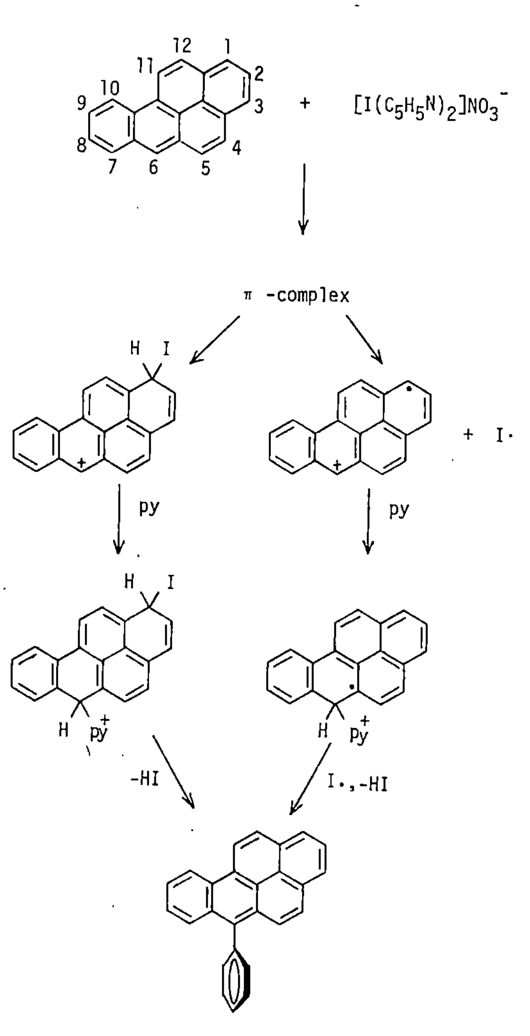
The formation of the 6-pyridinium derivative may be interpreted as arising *via* the proposed ionic mechanism with initial electrophilic attack occurring at position 1 or 3 rather than at position 6 as occurs in the formation of 6-iodobenzo[a]pyrene. The position of attack might change for steric reasons because different reagents could be involved as indicated by the following equilibria:

$$(py\text{-}I\text{-}py)^+ \rightleftharpoons (py\text{-}I)^+ + py \rightleftharpoons I^+ + 2\,py$$

If formation of 6-iodobenzo[a]pyrene arises from attack by I^+, the equilibrium in pyridine-chloroform will be displaced to the left and a bulkier reagent might attack at position 1 or 3, forming the 6-pyridinium derivative. Steric factors are important since acylation with succinic anhydride and alumium chloride gives the product with substitution in the one tion[4]. The excess pyridine present in the reaction mixture may also provide conditions where the addition of pyridine to the sigma complex formed by electrophilic attack at 1 or 3 is faster than the rate of elimination of a proton to give the 1- or 3-iodo derivative. The dihydro-disubstituted compound thus formed would then undergo elimination of HI to give the 6-pyridinium derivative.

The reaction can also be postulated to proceed *via* the radical cation of BaP. Although evidence has been found[3] that the radical cation of BaP, produced by oxidation with iodine, reacts with pyridine to give the 6-pyridinium derivative, no radical was detected under the conditions of these reactions. The simple iodine reaction does not proceed under the conditions employed in this study.

Both the ionic and radical modes are shown in the following reaction scheme.



The structural assignments for the iodo and pyridinium derivatives are based on the ultraviolet and 220 MHz nuclear magnetic resonance spectra (Fig. 1). The ultraviolet spectra match reported spectra for 6-iodobenzo[a]pyrene[5] and 6-pyridinium benzo[a]pyrene perchlorate[3]. The NMR assignments are based on comparison with the spectrum of the parent hydrocarbon[6,7], coupling constants, splitting patterns, and double resonance decoupling experiments. The NMR spectra of the pyridinium derivative establish the fact that the plane of the pyridine ring is perpendicular to the plane of the benzo[a]pyrene ring since protons 5 and 7 are shielded, relative to their positions in the parent compound, by the pyridine ring current. This is in contrast to the deshielding which all the protons, including 5 and 7, exhibit in the 6-iodo compound.

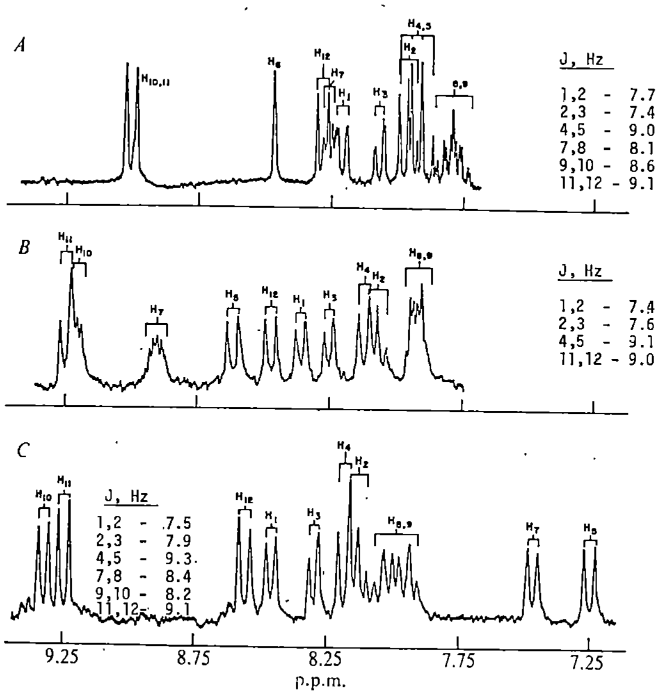


Fig. 1 220 MHz NMR spectra. *A*, Benzo[a]pyrene in $CDCl_3$; *B*, 6-iodobenzo[a]pyrene in tetrahydrofuran; *C*, the 6-pyridinium-d_5 derivative of benzo[a]pyrene in methanol.

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BIOLOGICAL SCIENCES

Evidence for Naturally Occurring Murine Sarcoma Virus

THE origin of the murine sarcoma viruses (MuSV) found in tumours resulting from the injection of mice with leukaemogenic viruses (MuLV)[1–3] and from spontaneous tumours[3,4] is very obscure. Viruses isolated from spontaneous tumours[3,4] might have been induced through accidental horizontal transmission of Moloney sarcoma virus. The origin of isolates of Moloney sarcoma virus[1,2] and Kirsten sarcoma virus[5] is also unknown because the virus preparations used had been passaged through rats[2,5] or mice of various strains for many years[1]. Nor is it known whether sarcoma virus was present in the preparations of murine leukaemia virus administered to the animals subsequently developing sarcomas. It has been suggested that Moloney MuSV is derived from Moloney MuLV[6], but there may be an endogenous, latent sarcoma virus present in mice which could perhaps be activated by the administration of a leukaemogenic virus. We now report that a clone-purified MuLV, isolated from an established cell line in tissue culture and having *in vitro* no demonstrable content of MuSV, induced sarcomas in several strains of mice and MuSV could be readily isolated from these sarcomas. The virus was also present in the plasma of the tumour-bearing mice.

The virus used was obtained from a clone of JLS–V9 cells[7] which, on routine passage, began to release spontaneously a murine leukaemia virus, positive in the XC assay[8]. Clone M4 was twice recloned following "turn-on" and the resulting chronically infected cell line served as the source of virus for this study. Cells were grown in Eagle's minimal essential medium with 10% heat-inactivated foetal calf-serum, penicillin and streptomycin. The tissue culture medium in which cells had grown was used as the stock of virus (JLS–V9MuLV) for these studies.

The cells used for the assay for transforming virus were 3T3 or TB cells. The latter were established from a mixed culture of thymus and bone marrow (J. K. B. and D. H., unpublished data) of CFW/D mice[9] using the procedure of Wright *et al.*[7]. The assay for MuSV focus forming units (f.f.u.) was carried out by mixing 1×10^6 cells in suspension with an equal volume of the appropriate dilution of virus in the presence of 'DEAE–dextran'[10]. The suspension was shaken at 37° C for 40 min and 2×10^5 cells plated. Medium was replaced two days post plating and the number of foci determined on the third day. In some experiments a simultaneous assay for MuSV XC activity was carried out as described above except that following infection 500 cells were plated. XC cells were added three days post infection and syncytium positive clones were counted on day 4.

Table 1 Effect of Input Multiplicity of Infection (m.o.i.) of Added MuLV on Titre of a Constant Number of Focus Forming Units

M.o.i. of MuLV	Titre (f.f.u. ml.$^{-1}$)	No. of determinations
30	1.5×10^5	2
15	2.0×10^5	2
8	2.7×10^5	3
4	6.8×10^5	6
2	12.9×10^5	6
1	14.5×10^5	6
0.5	9.0×10^5	3
0.25	5.5×10^5	3

Focus forming units (f.f.u.) assayed using TB cells.
The MuSV was a tissue culture harvest of cells (TB) infected with plasma from a mouse in which JLS-V9MuLV had produced a sarcoma.

Table 2 Incidence of Sarcomas Following Injection of JLS-V9MuLV into Various Strains of Mice

Strain	Group	Vol. injected (ml.)	No. of mice	No. of mice with tumours	Latent period (days)
CFW/D	I	0.05	55	50*	60–148
CFW/D	II	0.05	24	0	--
CFW/D	III	0.05	11	5†	70–90
CFW/D	IV	0.1	18	0	--
CFW/D	V	0.1	15	0	—
NIH Swiss‡	VI	0.05	18	16	50-150
C3H/Bi§	VI	0.05	10	5	40–110
C57Bl/6J‖	VI	0.05	11	5	50–190
CBA¶	VI	0.05	15	1	90

Group I, intraperitoneal injection into newborn mice.

Group II, injection directly into 7 day old thymus grafted under the kidney capsule of a normal, 6 week old recipient.

Group III, injection directly into 7 day old thymus grafted under the kidney capsule of recipients given 550 rad (whole body) before grafting.

Group IV, injection (intraperitoneal) into normal, 6 week old adults.

Group V, controls injected intraperitoneally with a compatible volume of tissue culture medium from noninfected JLS-V9 cells.

Group VI, intramuscular (thigh) injection into newborn mice.

* Includes 3 separate experiments using different tissue culture passage levels of JLS-V9MuLV.

† All tumours arose in muscle tissue underlying the kidney bearing the thymus graft or in the thigh (remote from site of injection).

‡ From NIH, Bethesda, Md.

§ From Dr H. S. Kaplan.

‖ From Jackson Laboratory, Bar Harbor, Maine.

¶ From MRC, Mill Hill.

Because the JLS-V9MuLV used in these studies was of high titre ($1-4\times10^8$) a very small content of MuSV might not be detectable by the focus assay. The measured titre of focus forming virus decreased when the multiplicity of MuLV surpassed an optimal level (Table 1). It was therefore necessary to dilute stock JLS-V9MuLV so that the input multiplicity of infection (m.o.i.) of MuLV was approximately two, and to infect enough cells to compensate for the dilution. The stock JLS-V9MuLV with 2×10^8 infectious units ml.$^{-1}$ (by XC assay) was diluted and mixed in suspension with 1.1×10^8 cells, all of which were plated at 2×10^5 cells per dish (60 mm diameter). The titre of MuLV in the medium three days post infection was 2×10^8, showing that the cells had been infected, but no foci were seen in any dish. In many experiments where JLS-V9MuLV has been grown in a variety of cell cultures, including primary and secondary mouse embryo cells of CFW/D, NIH Swiss, Balb/c and CBA we have never seen foci of transformed cells. To check the sensitivity of this focus assay we assayed a preparation of Moloney MuLV virus that appeared to be free of sarcoma virus when tested in the usual way. We found it to contain 480 focus forming units per ml. MuSV and 2×10^8 MuLV per ml.

The stock of JLS-V9MuLV that contained no detectable MuSV was injected into mice less than one day old. The results are given in Table 2. The intraperitoneal injection of JLS-V9MuLV into newborn mice or adult mice exposed to X-irradiation induced multiple tumours many of which appeared simultaneously. Tumours arose in muscle (all four limbs), peritoneal wall, diaphragm, along the spinal column, in the dermis and on the head and face. Histologically, they resembled the rhabdomyosarcomas or atypical granulomas described for those induced by MuSV (Moloney)[11] and MuSV (Harvey)[12]. In contrast to the latter tumours, the MuSV induced by JLS-V9MuLV produced no spleen enlargement in any of the tumour-bearing mice. All tumours grew progressively and killed their hosts. Transplantation to normal syngeneic adult mice resulted in initial tumour growth followed by complete regression, but in mice pretreated with 400 rad whole body irradiation there was progressive growth resulting in death of the animals. Tumours of this type have never been observed to occur spontaneously in CFW/D mice.

The undiluted virus stock resulted in a high tumour yield so the stock was diluted and injected intraperitoneally into mice less than one day old. The distribution of tumours and their biological behaviour, shown in Fig 1, was similar to that for the undiluted stock. If it is assumed that the tumour yield obtained with the 10^{-8} dilution of the virus was the result of a low level of MuSV present in the injected MuLV then the titre of such an MuSV would have been 1.6×10^8 f.f.u. per ml. (assuming that 1 f.f.u. would be sufficient to induce a tumour *in vivo*. The f.f.u. assay we used readily detected 480 f.f.u. ml.$^{-1}$ of MoMuLV(MuSV), and we therefore concluded that JLS-V9MuLV was free of transforming virus that can be detected *in vitro*.

To exclude the possibility that there was a small amount of pre-existing MuSV present in the JLS-V9MuLV which might have escaped detection *in vitro* but was selected for *in vivo*, the JLS-V9MuLV was clone purified. Cells of an established line (TB) were infected in suspension with

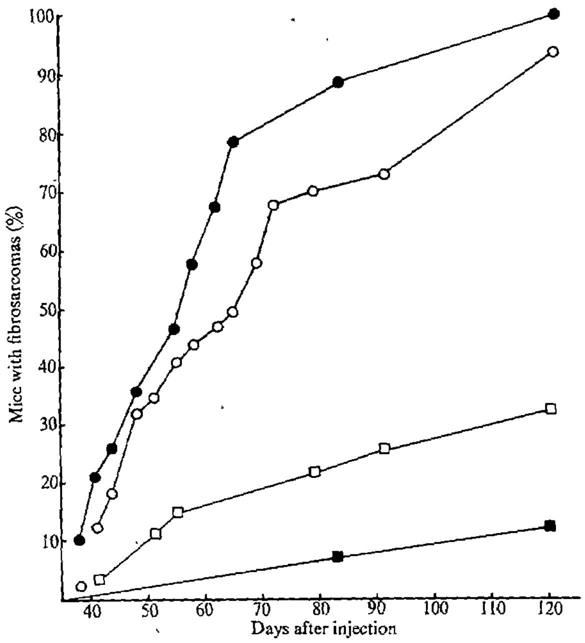

Fig. 1 Effect of dilution of JLS-V9MuLV on the incidence of fibrosarcomas in CFW/D mice. Newborn mice were injected with the following dilutions of tissue culture supernatant from chronically infected JLS-V9MuLV infected cells: ●, 0.05 ml. undiluted; ○, 0.1 ml. 10^{-1} dilution; □, 0.1 ml. 10^{-2} dilution; ■, 0.1 ml. 10^{-3} dilution. There were 24–34 mice per group.

a limiting dilution of JLS-V9MuLV and plated at 500 cells per plate. Three days post plating the medium was removed and replaced with medium containing 5×10^5 XC cells[8]. When these cells had attached (six hours after plating) the medium was replaced with medium containing 0.7% agar. The plates were incubated for a further 24 hours and then the agar immediately above an infected (XC positive) cell clone was picked and added to 1 ml. containing 1×10^5 normal TB cells in complete medium containing polybrene[13]. Following absorption the cells were plated, grown for three days when the medium was changed, and after a further 24 h the medium from a number of dishes, each infected with a different clone of JLS-V9MuLV, was collected and assayed for MuLV using the XC assay[14]. Five clones of JLS-V9MuLV were obtained having titres between $1.2–1.8 \times 10^8$, and each was tested by injecting approximately twenty newborn CFW/D mice with 0.1 ml. of cell-free tissue culture supernatant. All JLS-V9MuLV clones were positive for rhabdomyosarcoma induction by 45 days post infection. This shows that fibrosarcomas can be induced in mice by an MuLV which does not contain any MuSV.

Plasma from tumour-bearing mice and extracts of tumours[15] induced by JLS-V9MuLV were active *in vivo* for sarcoma induction in mice (NIH Swiss, Balb/c, CFW/D) and *in vitro* for both MuSV and MuLV activity. Assayed by the method of Hartley and Rowe[16] the plasma contained approximately 3×10^3 f.f.u. ml.$^{-1}$. Tumour extracts contained an average of 1×10^7 MuLV g^{-1} of tumour by the XC assay and 1×10^5 f.f.u. g^{-1} of tumour when assayed by the suspension-infection method described here. Such virus preparations were inactive when injected into newborn W/Fu rats (Microbiological Associates).

Only CBA mice proved refractory of all mouse strains tested, but this resistance was not found when CBA mice were injected with MuSV obtained from a JLS-V9MuLV induced tumour. Under these conditions CBA mice were as sensitive as CFW/D and NIH Swiss mice.

The results of a titration *in vivo* in CFW/D mice of plasma derived from mice bearing JLS-V9MuLV induced tumours are given in Table 3. Two different preparations of plasma were used in this experiment, but the data were pooled as both gave virtually identical results. The highest concentrations of virus resulted in rapid induction of tumours, whereas more dilute concentrations resulted in a high incidence of tumours with a long latent period. It appeared that there were two periods of time in which tumours arose in response to the injection of plasma, one with a short mean latent period with the high concentration of plasma and the other, separated from the first by a gap in time, with a mean latent period corresponding exactly with that found for tumours arising in mice injected with tissue culture preparations of JLS-V9MuLV.

Table 3 Incidence and Average Latent Period of Neonatal Sarcomas (CFW/D Mice) induced by Plasma from Mice Bearing Tumours Induced with JLS-V9MuLV

Plasma dose	Volume (ml.)	Mice*	Tumours*	Average latent period (days)†	% Tumours
Undiluted	0.05	13	13	21*	100
10^{-1}	0.1	20	20	20	100
10^{-2}	0.1	32	24	26	
			8	$53 \begin{smallmatrix} \diagup 52\ddagger \\ \diagdown 58 \end{smallmatrix}$	100
10^{-3}	0.1	28	4	21	
			21	$72 \begin{smallmatrix} \diagup 48 \\ \diagdown 150 \end{smallmatrix}$	90

* One mouse developing a tumour on day 94 excluded from group.
† Time to first appearance of tumour.
‡ Times at which earliest and latest tumours appeared.

The results of these experiments suggest that, first, a focus forming virus is responsible for the early arising tumours and, second, a virus which can activate a sarcoma inducing activity is responsible for the late appearing tumours. Experiments are in progress to correlate the levels of these two viral activities with early and late appearing tumours, and preliminary data suggest there is a correlation.

To explain the experimental results obtained we suggest that JLS-V9MuLV could function by: (1) containing the necessary genetic information for MuSV which can be expressed *in vivo* but not *in vitro*, (2) JLS-V9MuLV can "activate" a latent endogenous MuSV, (3) JLS-V9MuLV might recombine genetically with oncogenic information[17] *in vivo*. We are now testing these models. Studies of the relationships between MuLV and MuSV should be aided by the reproducible recovery of MuSV directly from animals, thus avoiding passage through animals and/or tissue culture.

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Puromycin Stimulation of Rat Liver Ornithine Decarboxylase Activity

It is well known that puromycin inhibits protein synthesis in mammalian systems[1], but other metabolic effects have been reported[2–5]. Our own work on the purification of rat liver ornithine decarboxylase (ODC)[6], the apparent rate-limiting enzyme in polyamine synthesis, led us to a study of hormonal factors which alter the activity of this enzyme. We found that dibutyryl-cyclic adenosine 3′,5′-monophosphate (dibutyryl-cyclic AMP) stimulated hepatic ODC activity in normal rats[6a]. When actinomycin D, which had no independent effect on the basal level of the enzyme, was given with dibutyryl-cyclic AMP, ODC activity was inhibited. However, when the animals were dosed with either puromycin alone or puromycin and dibutyryl-cyclic AMP at levels of puromycin which inhibited protein synthesis, the antibiotic alone stimulated ODC activity and potentiated the activity due to dibutyryl-cyclic AMP.

The effect of a single intraperitoneal administration of puromycin to normal rats indicates a clear stimulation of hepatic ODC activity, reaching a peak of 71.7 units (U) after 3.5 h, a more than fourteen-fold increase over zero time controls (Fig. 1*A*). The activity then fell off to 15.2 U, or slightly more than 20% of the 3.5 h activity. Fig. 1*A* shows that saline had no effect of its own; these latter values varied, as did the non-injected control values, between 2.2 and 11.5 U during 5 h. This figure also shows that a single intraperitoneal administration of dibutyryl-cyclic AMP to normal rats stimulated hepatic ODC activity. Peak activity occurred 2–3 h after dosing, and this was an earlier maximum response than that seen after puromycin administration. Two hours after dosing with dibutyryl-cyclic AMP, the ODC activity was 40.3 U, a more than eight-fold increase over the zero time value of 4.9 U. The dibutyryl-cyclic AMP-stimulated ODC activity increased slightly to 44.6 U by 3 h and then fell to values ranging from 12.2 to 14.5 U between 3.5 and 5 h after drug administration.

The synergistic effect of dibutyryl-cyclic AMP and puromycin is seen when these two compounds are administered concurrently. Whereas at 2 h a preliminary decrease in ODC activity was seen (10.9 U, a 73% decrease compared with animals given dibutyryl-cyclic AMP alone), by 3 h the ODC activity was 167 U. This greater than thirty-five-fold stimulation over the zero time value was more than additive, since the combined activities of the dibutyryl-cyclic AMP and puromycin alone were 79.3 U. The peak puromycin dibutyryl-cyclic AMP-stimulated activity (175 U at 3.5 h) occurred when the dibutyryl-cyclic AMP-stimulated activity had returned to 13.2 U. The puromycin/dibutyryl-cyclic AMP-stimulated activity then decreased to 48.9 U by 5 h, a value equivalent to the maximum activity obtained with dibutyryl-cyclic AMP alone (44.6 U).

We tried to correlate the time sequence of inhibition of protein synthesis by puromycin with the stimulation of ODC activity. Puromycin or puromycin plus dibutyryl-cyclic AMP depressed protein synthesis by more than 60% after 1 h (Fig. 1*B*), at a time when no differences in ODC activity were discernible (Fig. 1*A*). However, Fig. 1*B* shows that the ODC activity increased and reached a maximum when

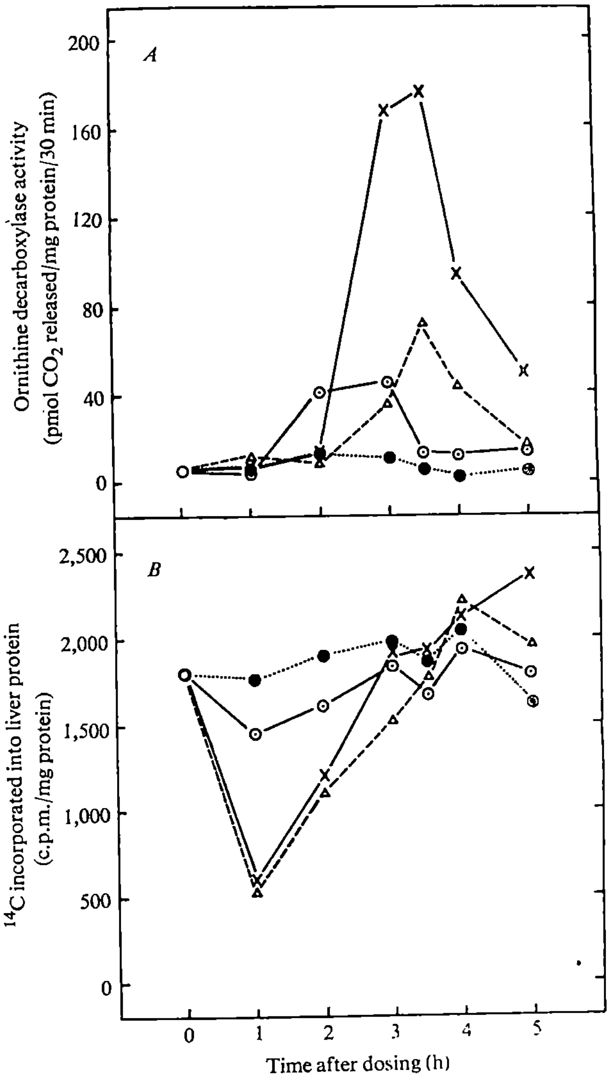

Fig. 1 Effect of puromycin and dibutyryl-cyclic AMP on (*A*) rat liver ornithine decarboxylase activity and (*B*) radioactivity from ^{14}C-leucine injection incorporated into total liver protein. Male, Sprague-Dawley rats (140–160 g) were used, and chemicals were obtained from commercial sources. The rats were fasted overnight, with a minimum of 15 h of food deprivation before death. Rats were injected intraperitoneally at zero hours with either puromycin (△), 12 mg in 0.2 ml. isotonic NaCl; neutralized/100 g body weight, dibutyryl-cyclic AMP (○), 2 mg in 0.2 ml. isotonic NaCl/100 g body weight, puromycin + dibutyryl-cyclic AMP (×), or isotonic NaCl (●), 0.2 ml./100 g body weight. *A*, The preparation of the 100,000*g* supernatant fraction and the assay of ODC activity by trapping $^{14}CO_2$ released from (1-^{14}C)-DL-ornithine have been described (refs. 6 and 6a). One unit of enzyme activity is expressed as pmol $^{14}CO_2$ released per mg protein per 30 min. Protein was measured by the biuret method[7], using bovine albumin as a standard. The results presented for each point represent the mean of three to eight animals; each individual assay was done in triplicate. The standard errors varied from 15 to 20% in all cases, and the statistical analysis of the data was determined using the *t* test. *B*, All animals received an intraperitoneal injection of 15 μCi/100 g body weight (1-^{14}C)-L-leucine (28.7 mCi mmol) 20 min before killing. It was ascertained experimentally that the ^{14}C-leucine administered to the rats did not interfere with the assay of ODC activity. To determine the amount of ^{14}C incorporated into liver protein, aliquots of the whole homogenate were precipitated with 5% trichloroacetic acid (TCA), heated at 80–90° C for 15 min, cooled and centrifuged. The samples were washed twice in 5% TCA, extracted with hot ethanol (70° C for 15 min), centrifuged, resuspended in TCA and centrifuged again. The pellets were dissolved in 0.1 N NaOH and aliquots were counted for radioactivity. Protein was measured by the method of Lowry *et al.*[8], using bovine albumin as a standard.

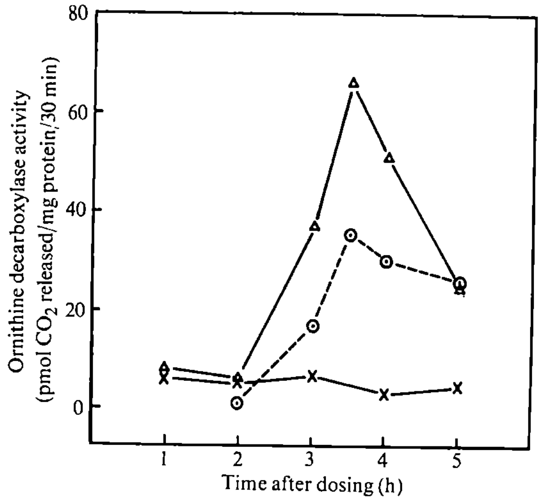

Fig. 2 Effect of puromycin and actinomycin D on rat liver ornithine decarboxylase activity. Conditions were as in Fig. 1. Rats were injected intraperitoneally with either puromycin (△), 12 mg in 0.2 ml. isotonic NaCl, neutralized/100 g body weight, actinomycin D (×), 80 µg/100 g body weight (the drug was dissolved in a minimal volume of 50% ethanol and brought to volume with 0.9% NaCl), or puromycin+actinomycin D (⊙). As in Fig. 1*A*, one unit of enzyme activity is expressed as pmol $^{14}CO_2$ released per mg protein per 30 min. The results presented for each point represent the mean of three to eight animals, and the standard errors ranged from 5 to 25% in all cases. The dose of actinomycin D was selected as the optimal dose which prevents any increase in incorporation of ^{14}C-orotic acid into hepatic nuclear and cytoplasmic RNA[13].

the puromycin inhibition of protein synthesis was terminated (3 h); dibutyryl-cyclic AMP slightly depressed protein synthesis, but this was not statistically different from controls.

The effect of actinomycin D on the puromycin-stimulated ODC activity was to reduce the peak at 3.5 h by 47% (Fig. 2). However, the increase in ODC activity was still appreciable at this time (35.4 U). The decline of enzyme activity from livers of animals treated with these drugs was less rapid than that seen with the enzyme from animals treated with puromycin alone, an activity of 75% (25.4 U) of peak values being reached by 5 h. Fig. 2 also shows that actinomycin D alone had no stimulatory effect on hepatic ODC activity.

We may consider some explanations for the puromycin effect. If the assumption is made that there exists a protein inhibitor of ODC which is more sensitive than ODC to the actions of puromycin, then after the administration of the drug, at a time of maximal depression of protein synthesis, the production of both the inhibitor protein and the ODC would cease. However, as puromycin levels decrease, protein synthesis would resume, but the inhibition of ODC would be relieved first, thus causing a rise in ODC activity. Alternatively, it may be possible that because puromycin causes an extensive inhibition of protein synthesis, this produces an accumulation of the ODC messenger RNA, subsequently resulting in a "rebound" phenomenon of greatly enhanced ODC activity when the drug effect was terminated. Both of these hypotheses are consistent with the kinetics of inhibition presented in Fig. 1 and are amenable to experimental verification.

Such facile explanations, however, should be tempered by the complexities inherent in the metabolism of eukaryotic cells, and other explanations for the puromycin effect are possible. For example, partial hepatectomy results in an increased amino-acid content of hepatic cells[9–11]; at the same time, ODC activity increases[12–18]. In addition, cyclic AMP increases the hepatic content of free amino-acids[19], and administration of dibutyryl-cyclic AMP[6a] or a mixture of amino-acids[13] increases ODC activity. It is thus conceivable that the inhibition of protein synthesis by puromycin also increases hepatic amino-acid pools which then act as a causal stimulus for increased ODC activity.

Other possibilities may be considered. (*a*) Puromycin may increase endogenous levels of cyclic AMP with consequent increases in ODC activity; such an explanation has been proposed for changes in the activities of glycolytic enzymes by puromycin[3,20]. However, the same dose of actinomycin D which completely inhibits the dibutyryl-cyclic AMP stimulation of ODC activity[6a] only partially inhibits the puromycin effect. (*b*) The drug may release nascent polysomal ODC molecules. It is known that both cyclic AMP and puromycin can release nascent protein and active enzyme from polysomes *in vitro*[21,22], but these effects were not found *in vivo*[23]. Furthermore, this explanation might require the peak in ODC activity to occur at the time of the maximum effect of puromycin on protein synthesis; this, as has been shown, is not the case. (*c*) It has been shown that steroids increase ODC activity (refs. 6a, 24 and 25). Thus it is possible that puromycin administration stresses the animals severely enough to cause the release of adrenal cortical hormones. All these considerations are suitable for experimental investigation.

Finally, the enhancement of ODC activity in normal rats should not be confused with the "paradoxical" effect of puromycin in augmenting the already high enzymatic activities of foetal tissues or of hydrocortisone-stimulated preparations[23,26–29]. Whereas a low dose of actinomycin D inhibits the puromycin-stimulated ODC activity (Fig. 2), the drug has been shown to "super-induce" tyrosine aminotransferase in tumour cells[30,31].

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Cholinesterase Inhibitors: Structure of Eserine

ESERINE (physostigmine) was first isolated from the Calabar bean in the latter half of the last century[1], but it was not until much later that its activity on the heart was demonstrated to be due to inhibition of acetylcholinesterase[2,3]. It is one of the few compounds that are equally active as inhibitors of both true and pseudo-cholinesterase and has been used by many workers as a reference standard in the evaluation of new cholinesterase inhibitors. The chemical structure of this alkaloid was elucidated by Stedman[4] and the absolute configuration has relatively recently been confirmed by use of the nuclear Overhauser effect (NOE) in NMR spectroscopy[5]. As part of our study of the geometry of molecules affecting cholinergic nervous transmission, we have determined the crystal structure.

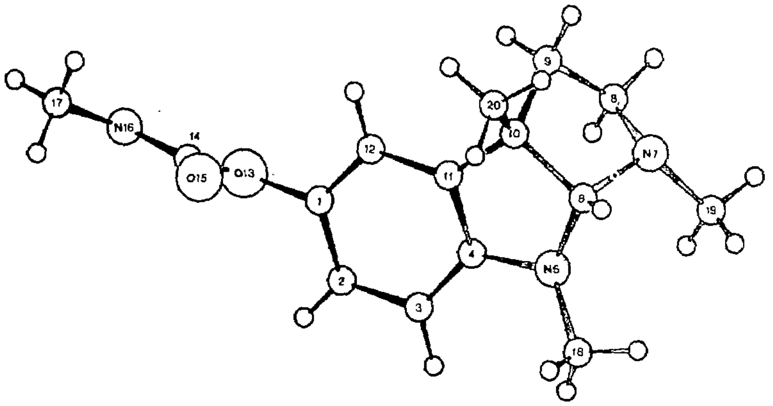

Fig. 1 Perspective drawing of eserine, projected on the plane of N5–N7–C9–C11. The absolute configuration corresponds to that of the natural alkaloid.

Crystals of eserine (BDH Ltd), as clear tabular plates, are orthorhombic, space group $P2_12_12_1$, with $a=1458$ (1), $b=1435$ (1), $c=727.1$ (6) pm. Three-dimensional intensity data were measured on a computer-controlled[6] four-circle diffractometer using graphite monochromatized MoK_α radiation. 2,658 measurements for $2\theta \leq 60°$ yielded 2,556 symmetry-independent observations, of which 1,520 were significantly above background ($I \geq 3\sigma(I)$). The structure was solved by application of multi-solution direct methods and refined by block-diagonal least squares using anisotropic temperature factors for C, N and O, and isotropic vibrations for hydrogen. The present values of R are 0.060 over the 1,520 significant reflexions and 0.097 over all 2,531 data.

The conformation of the molecule is shown in Fig. 1, in the absolute configuration corresponding to that of the natural alkaloid. The two pyrrolidine rings are *cis*-fused, and that adjacent to the aromatic ring is practically flat, while the other is in the half-chair (C_2) conformation with the two-fold axis passing through C8 and the centre of the C6–C10 bond. Both ring nitrogen atoms are tetrahedral, but N5 is rather flattened and has more sp^2 character, judging from the bond angles. The C18 methyl group is *cis* to the hydrogen on C6, in agreement with the results of the NOE study[5]. In solution there is no inversion of configuration by C18 and the lone pair on N5 (ref. 5), but the second pyrrolidine ring may be expected to be conformationally rather flexible because of inversion through N7. In the crystal, the lone pair on N7 is also *cis* to the hydrogen atom on C6. The carbamate group is planar, with the hydrogen on N16 *trans* to the keto oxygen, and will remain so in solution because of the partial double bond C14–N16. In the crystal, the torsion angle C12–C1–O13–C14 is observed to be −72°, but an examination of CPK space-filling atomic models indicates that this angle may range −30° to −150° and +30° to +150°: the value of 31.8 observed by us in the crystal structure of neostigmine bromide[7] is clearly a lower bound and no sign of a similar interaction between the *ortho* aromatic proton and the keto oxygen exists in the present structure.

Chothia and Pauling[8] have postulated a particular conformation of acetylcholine as being the conformation relevant to interaction with the esterase, and Pauling and Petcher[7] have pointed out the similarity between this postulated conformation and the observed solid-state conformation of neostigmine. It is difficult to correlate the conformation of eserine with these two because of the *para* relationship of N5 and the carbamate group in eserine. The observed conformations of eserine and neostigmine are, however, similar in some respects. The N5–C14 and N5–O15 distances are 638 and 620 pm respectively, compared with 605 and 647 pm in neostigmine. AChE appears to be relatively insensitive to molecular shape as far as reversible inhibition is concerned, provided that three necessary groups are present, these being a carbamate group bonded to an aromatic ring which must carry an alkyl substituted nitrogen atom in the *meta* or *para* position.

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Circulating Sensitized Lymphocytes in Systemic Lupus Erythematosus

SYSTEMIC lupus erythematosus (SLE) is a classical autoimmune disease in man associated with the presence of autoantibodies to DNA and other self-antigens[1]. It is not clear whether specifically sensitized lymphocytes active as effector cells of cell-mediated immunity (CMI) to DNA are also present. Inhibition of leucocyte migration[2,3], lymphocyte transformation in the presence of DNA[4,5] and destructive effects of lymphocytes from SLE against human cells *in vitro*[6] have been reported. It has also been claimed that lymphocytes in SLE are unresponsive to mitogens[7] and that an inhibitor of leucocyte migration reflects depressed CMI[8].

Here we report the direct cytotoxic activity of peripheral blood lymphocytes from SLE against target cells coated with DNA. We consider that this complement independent cytotoxicity probably reflects the activity of T lymphocytes in man, by analogy with experiments in mice[9,10].

We examined four women with a typical clinical picture of SLE. Three were in an active stage with LE cells in the blood and antinuclear antibody, while the fourth (M. M.) was in remission and immunologically inactive without anti-DNA antibody (see Table 1). Patient F. L. showed splenomegaly with thrombocytopenic purpura, the other three cases had connective tissue disturbances.

The results and experimental details are shown in Table 1. Lymphocytes were incubated with control target cells without antigen, and with target cells coated with purified tuberculin, microsomal fractions of human thyrotoxic glands, human thyroglobulin, and DNA. Cytotoxic activity of the lymphocytes was demonstrated in all patients in an active stage of SLE: against DNA antigen in patients F. L. and Ch. E., and against TG antigen in patients F. L. and P. Y. One patient, Ch. E., showed a very high specific cytotoxic activity of the peripheral lymphocytes directed only against DNA coated cells. Tests for thyroid autoantibodies were negative in patients F. L. and P. Y., and antinuclear antibodies were detectable in the absence of cytotoxic activity to DNA coated target cells in P. Y. In the one case of SLE in remission no cytotoxic activity of lymphocytes was detected, neither were antibody or LE cells present. The effect of addition of rabbit antiserum against human lymphocytes to the incubation mixtures of lymphocytes, from patient P. Y., with DNA coated target cells is shown in Fig. 1. The cytotoxic activity of the lymphocytes was strongly inhibited in comparison with control normal rabbit serum.

Autoantibodies are important in the pathogenesis of the disorders of SLE[1]. Lymphocytes sensitized to self antigen may also occur and affect the disease process. It has been claimed that the skin lesions of SLE resemble the changes seen in delayed-type hypersensitivity[11]. Direct cytotoxicity of lymphocytes on allogenic cells in the absence of complement has been shown to be mediated by T cells in mice[9,11]. Similar cytotoxic activity of human lymphocytes in the absence of complement has been considered to be dependent on T cells[12]. Direct proof of T cell involvement is not possible in the absence of specific antiserum to human T cells, but the inhibition of cytotoxicity by ATS in these experiments also suggests T cell participation. The presence of sensitized T cells in SLE and other autoimmune diseases raises two important possibilities. First, such lymphocytes could be directly cytotoxic *in vivo* to any cells carrying the appropriate antigen on their surface. In this way sensitized lymphocytes might participate in lesions. Second, these lymphocytes could function as "helper" cells[13], cooperating with B cells, and might initiate antibody production.

There is evidence that in SLE the appearance of antibodies to DNA follows chronic bacterial[14] or viral[15] infections. It

Table 1 Comparative Results in Systemic Lupus Erythematosus

Patient	Sex	Age	Antinuclear antibodies*	Thyroid antibodies		LE cell phenomena	Lymphocytes§ incubated with mastocytoma‖ target cells¶				
				TRC†	CFT‡		*a*, Non-coated	*b*, Coated PPD	*c*, Coated MC	*d*, Coated DNA	*e*, Coated TG
F. L.	F	51	Positive	Negative	Negative	Positive	4.04	6.25	7.16	14.64	37.57
Ch. E.	F	46	Positive	**	**	Positive	0.92	7.72	2.79	40.99	2.17
M. M.	F	51	Negative	**	**	Negative	2.24	6.30	1.46	0.00	0.00
P. Y.	F	23	Positive	1/25	Negative	Positive	4.09	8.29	5.86	6.24	21.98
			Controls				Mastocytoma target cells				
			With normal lymphocytes (n = number of donors)			n =	12	11	14	8	12
						$\bar{x}$ =	2.55	5.34	3.38	2.30	3.75
						s.e.m. =	0.76	0.92	0.80	0.90	0.99

* Detected using immunofluorescence technique.

† Haemagglutinin antibody titre determined by thyroglobulin haemagglutinating test (TRC).

‡ Complement fixing antibody titre determined by thyroid complement fixing antigen (CFT).

§ Prepared from defibrinated blood containing 100 mg per 10 ml. carbonyl iron powder. Separation by sedimentation, following 1 h incubation at 37° C, in 3% dextran and Eagle's medium containing 10% inactivated calf foetal serum (CFS). Lymphocytes were washed three times, iron particles and phagocytic cells removed and erythrocytes lysed when necessary by 0.83% ammonium chloride. Lymphocytes were 95±2% pure.

‖ Mouse P-815 mastocytoma cells (DBA/2 strain) labelled with sodium chromate 51 (1 mCi ml.$^{-1}$; specific activity 200–700 mCi mg^{-1} chromium). Labelled cells (2×10^6) suspended in 0.5 ml. Tris buffered saline, *p*H 7.2 and incubated for 1 h with 0.5 ml. of 2 mg ml.$^{-1}$ ECDI (N-ethyl-N′-(3-dimethylamino-propyl)-carbodiimid-HCl). Excess antigen removed by washing six times with Eagle's medium.

Cells coated with 2 ml. of: 2.5 mg ml.$^{-1}$ herring sperm DNA; 2.5 mg ml.$^{-1}$ human thyroglobulin (TG); 350 μg ml.$^{-1}$ microsomal fractions of human thyrotoxic glands (MC); 500 μg ml.$^{-1}$ purified tuberculin (PPD). Cell viability was tested with trypan blue.

¶ One ml. of 2.5×10^6 cells ml.$^{-1}$ lymphocytes mixed with 0.1 ml. viable target cells 5×10^4 cells ml.$^{-1}$. After mixing with 5% CO_2 in air and incubation in sterile sealed tubes at 37° C for 15 h, they were centrifuged for 5 min at 1,500 r.p.m. Assay of supernatant for ^{51}Cr used a deep-well scintillation counter. Results expressed as "cytotoxic index":

$$\frac{\text{Experimental } ^{51}\text{Cr release} - \text{spontaneous } ^{51}\text{Cr release}}{\text{Maximal } ^{51}\text{Cr release} - \text{spontaneous } ^{51}\text{Cr release}} \times 100$$

Maximum release of ^{51}Cr from labelled target cells incubated in distilled water was 82%, spontaneous release in Eagle's medium with CFS was 19±3%.

** Not measured.

is also possible that autocytotoxins to lymphocytes[16] may result in enucleation of lymphocytes and the expression of self-DNA. Such mechanisms may explain the emergence of sensitized lymphocytes as a response to either non-self DNA antigens. The presence of lymphocytes sensitized to self antigen in SLE has a counterpart in Hashimoto's disease, where lymphocytes sensitized to thyroglobulin have also been demonstrated[12].

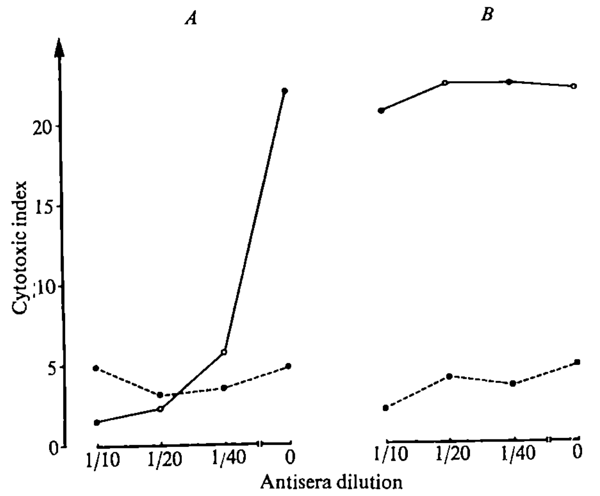

Fig. 1 Inhibitory action of rabbit antiserum against human thymocytes. Rabbit antiserum against human lymphocytes (*A*) and control rabbit serum (*B*) were inactivated for 30 min at 56° C and absorbed with human AB, Rh+ red blood cells. ○—○, Lymphocytes from SLE (P. Y.); ● - - - ●, normal lymphocytes.

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Chronoperiodicity in the Response to the Intra-amniotic Injection of Prostaglandin F$_{2\alpha}$ in the Human

CIRCADIAN rhythms in susceptibility to drugs are well documented, both in laboratory animals and man, and as a consequence the concepts of circadian chronopharmacology, chronotoxicology and chronotherapy have developed[1]. Although there is a most marked circadian rhythm in the incidence of spontaneous delivery in women[2], there appear to have been no studies of the chronopharmacology of drugs, such as oxytocin and the prostaglandins, used in the induction of labour or abortion.

In a study of factors influencing the induction–abortion interval following the intra-amniotic injection of prostaglandin F$_{2\alpha}$ (PGF$_{2\alpha}$), it became obvious that there was an association between the duration of this interval and the time of injection. This communication reports the results from a study of sixty nulliparous and thirty parous women, between the 12th and 20th weeks of gestation, concerning the relationship between the time of injection of PGF$_{2\alpha}$ and the subsequent interval to abortion.

This study was carried out during the period March–July 1972 using a standardized procedure in which PGF$_{2\alpha}$ was injected transabdominally into the amniotic sac in a dose of 30 mg, followed, if necessary, by doses of 15 mg at 24 h and 42 h. All the patients were admitted to hospital at least 4 h before treatment and were allowed to eat at the normal meal times of 7 a.m., midday and 5 p.m. The PGF$_{2\alpha}$ treatment was initiated at various times within the period 8 a.m. to 10 p.m.

No other drugs except pethidine (for analgesia) and metoclopramide or 'Debendox' ('Debendox' [Wm. S. Merrell]: dicyclomine hydrochloride 10 mg, doxylamine succinate 10 mg, pyridoxine hydrochloride 10 mg, for nausea and vomiting) were administered between the time of admission and subsequent abortion.

Table 1 Effect of Time of Intra-amniotic Injection of PGF$_{2\alpha}$ upon Subsequent Induction–Abortion Interval

Parity of patient	Mean induction–abortion interval (hours $\mp$s.e.)		Significance of difference $P<$
	6 p.m. injection	Injection at all other times within 8 a.m.–10 p.m. period	
Nulliparous	10.5$\mp$1.1 (8)	28.0$\mp$1.6 (52)	0.001
Parous	10.3$\mp$1.8 (6)	22.1$\mp$1.8 (24)	0.005
Total patients	10.4$\mp$1.0 (14)	26.2$\mp$1.3 (76)	0.001

The number of patients is shown in parentheses.

The induction–abortion interval was found to be significantly influenced by both parity of the patient and the time of administration of PGF$_{2\alpha}$. The mean induction–abortion interval ($\mp$s.e.) for parous women, 19.7$\mp$1.7 h, was less ($P<0.05$) than that for nulliparous women, 25.6$\mp$1.6 h. The induction–abortion interval was shortest when the initial injection of PGF$_{2\alpha}$ was administered at 6 p.m. (Table 1) and showed a distinct chronoperiodicity in nulliparous women (Fig. 1). There was no apparent relationship between the duration of the induction–abortion interval and stage of gestation, medication with drugs, time of hospitalization or time of eating.

In the nulliparous group, the mean induction–abortion interval was significantly less following PGF$_{2\alpha}$ administration at 5 p.m.–7 p.m. than at any other time (compare 8 a.m.–10 a.m., 8 p.m.–10 p.m. and all times except 5 p.m.–7 p.m., $P<0.001$; cf. 11 a.m.–1 p.m., $P<0.005$; cf. 2 p.m.–4 p.m., $P<0.01$) and was significantly less ($P<0.001$) at 6 p.m. than at either 5 p.m. or 7 p.m. (Table 2).

These findings have immediate clinical implications because

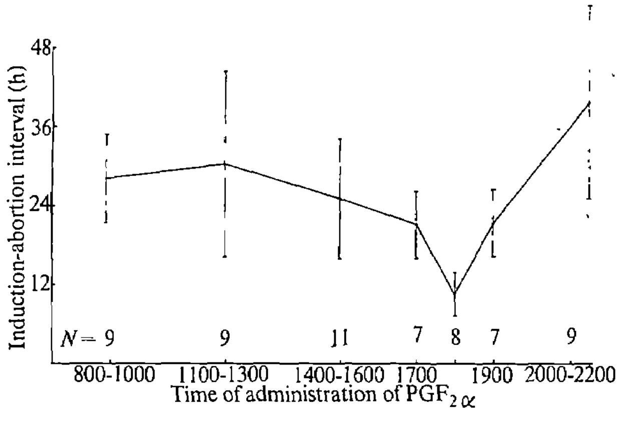

Fig. 1 Relation of time of intra-amniotic injection of $PGF_{2\alpha}$ to induction–abortion interval in nulliparous women (mean ±s.e.).

the induction–abortion interval influences the total dose of $PGF_{2\alpha}$ administered, the duration of hospitalization and the duration of exposure to side-effects of $PGF_{2\alpha}$ (which can be quite unpleasant). Further, a protracted induction–abortion interval produces severe anxiety in most patients. In terms of the total dose of $PGF_{2\alpha}$ required to terminate the pregnancy, there is a highly significant difference ($P < 0.002$) between the group treated at 5–7 p.m. and the group treated at other times: of those treated at 5–7 p.m., 74% required only a single dose of 30 mg whereas 63% of those treated at other times required a total dose of 45 mg or more. None of the patients treated at 6 p.m. required more than the initial dose of 30 mg of $PGF_{2\alpha}$. Although a not inconsiderable percentage (43%) of women injected at 6 p.m. aborted within 8 h, no women injected at any other time aborted in less than 9 h.

Table 2 Chronoperiodicity in Response to the Intra-amniotic Injection of $PGF_{2\alpha}$ in Nulliparous Women

Time of injection	Number of patients	Induction–abortion mean ∓ s.e.	Interval (h) range
8 a.m.–10 a.m.	9	28.0 ∓ 2.3	19.25–45.0
11 a.m.–1 p.m.	9	30.2 ∓ 4.7	9.1–51.8
2 p.m.–4 p.m.	11	25.1 ∓ 2.7	13.25–43.74
5 p.m.–7 p.m.	22	17.3 ∓ 1.4	6.0–28.5
8 p.m.–10 p.m.	9	39.7 ∓ 4.9	12.0–61.0
All times except 5 p.m.–7 p.m.	38	30.5 ± 2.1	9.1–61.0

Because the duration of the induction–abortion interval is an individually unique rather than a recurrent parameter, it might be expected to be difficult to demonstrate a circadian rhythm; nevertheless, the present observations establish unequivocally that the duration of this interval is a chronoperiodic phenomenon. In view of the fact that intra-amniotically injected $PGF_{2\alpha}$ appears to be slowly transferred from the amniotic compartment[3], it would seem remarkable that a difference of 1 h in either direction from 6 p.m. can double, or increase by more than 10 h, the mean induction–abortion interval.

The observed periodicity in response to the intra-amniotic injection of $PGF_{2\alpha}$ must, undoubtedly, be related to endocrine and/or other rhythmic metabolic changes. Although it would be premature to speculate concerning the factors involved in the chronoperiodicity of this response, the similarity of the pattern of response to the intra-amniotic injection of $PGF_{2\alpha}$ to that of the circadian rhythm in salicylate excretion time[4] is too obvious to avoid comment; the salicylates have been shown[5] to inhibit prostaglandin synthesis and release.

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Papilloma Induction in Different Aged Skin Grafts to Young Recipients

THE incidence of malignancy in lymphoid tissue increases with age in BALB/c mice[1]. This could reflect either a deterioration of the immune surveillance mechanisms of the animals or there may be an increasing rate of malignant transformation of lymphoid cells with increasing age. Some evidence for the latter suggestion has been obtained by transferring lymphoid cells from old and young non-malignant syngeneic donors to young BALB/c recipients. Reticular tumours developed with an incidence that was three times higher in recipients of old cells than in mice which received young cells[1]. Interpretation of my results, however, was limited by an inability to determine whether the tumours were derived from donor cells or host cells. In an attempt to overcome this problem I have investigated here tumour development on skin grafts transferred from old and young syngeneic donors to young recipients. Inbred BALB/c mice were used. A dorsal skin graft measuring 2 × 3 cm was placed on the back of each recipient with the graft hair pointing in the opposite direction to that of the recipient hair. Donor and recipient were of the same sex. All recipients were 2 months old when grafted and the donors either 14 or 2 months old. Twelve months later 25 μl. of acetone containing 40 $\mu g\ ml.^{-1}$ of 7,12-dimethylbenz[α]-anthracene (DMBA) was applied once to the depilated graft. The phase of the hair cycle was checked before treatment with DMBA by observing the growth (or absence of growth) of the hair stubs for 5 days after dyeing the hair. Papillomas first appeared on the grafts 4 weeks after the application of DMBA, and 3 weeks later the maximum number of papillomas had appeared. Approximately 60% of grafts from old donors and 25% of grafts from young donors bore papillomas (Table 1). Five months after DMBA treatment 80% of papillomas had regressed. Two months after the application of DMBA four carcinomas appeared on skin from an old donor and one on the skin from a young donor. No tumours developed on 35 male and 30 female mice bearing skin grafts treated with acetone only. This indicated an age dependent susceptibility of skin to a chemical carcinogen. The recipient mice were all of the same age, so that a decline in immune responsiveness with advancing age[2–4] alone could not account for the difference in susceptibility of skin from old and young donors. Although the growth cycle of hair can greatly influence chemical carcinogenesis[5–7], the number of mice in resting phase or growth phase was approximately the same in all groups, and I suggest that my results were not affected by this factor. The rate of skin sebum secretion may decrease with age and result in retention of a higher proportion of the applied carcinogen than in younger animals[7]. This may have increased the sensitivity of skin from old mice. It is unlikely to be the sole cause, as results have been obtained with lymphoid

Table 1 Papillomas on DMBA-treated Skin Grafts from Old and Young Syngeneic BALB/c Mouse Donors

Number of mice	Sex	Donor age when trans-planted (months)	Graft age when DMBA treated (months)	Number of grafts in resting growth phase when DMBA treated	Number of papil-lomas	Number of carci-nomas
24	M	14	26	11	12 (50%)	2
28	F	14	26	16	18 (64%)	2
15	M	2	14	7	2 (16%)	
34	F	2	14	18	10 (29%)	1

tumours[1]; lymphocytes transferred from old donors to young recipients resulted in a higher incidence of spontaneous lymphoid tumours than transfer from young donors.

My results suggest that the toxicity of a chemical carcinogen may differ to a degree, depending on the age of the tissue it contacts. The ages of those employed in potentially carcinogenic environments would have to be considered in greater detail if this is proved to be correct.

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Stereoselectivity and Differential Metabolism *in vivo* of Dextro and Laevo-Methadone-1-^{3}H

MORPHINE-LIKE analgesics which exist as two or more optically active enantiomorphs are known to exert their pharmacological action exclusively or preponderantly in one configuration[1]. Dextro-isomers are generally inactive with respect to analgesia and effects on respiration and do not produce physical dependence in contrast to the pharmacologically active laevo-enantiomorphs. Optical isomers therefore have potential for the elucidation of basic mechanisms concerned with pharmacological effects. Previous studies on *d*- and *l*-isomers of methadone[2–4] (Fig. 1), racemorphan[5–7], zocine[8], and prodine[9] have not shown any meaningful delineations in absorption, regional distribution or metabolism of these isomers. Stereoselective events at the hypothetical asymmetric analgesic receptor have generally been postulated as the chief mediator of molecular specificity[10–13]. Together with previous work on *l*-methadone (refs. 14, 15 and A. L. M., S. J. M., J. R. Bloch and N. L. Vadlamani, submitted for publication) we show here for the first time that the observed enantiomeric potency differences between *d*- and *l*-methadone-l-^{3}H could be attributed to (1) the formation of an apparently active metabolite in rat brain with *l*-methadone[14], but not with *d*-isomer; (2) significant differences in half-lives of these isomers in rat brain and plasma; (3) differential stereoselective N-dealkylation pathway being a major route of metabolism with *l*- but not with *d*-isomer.

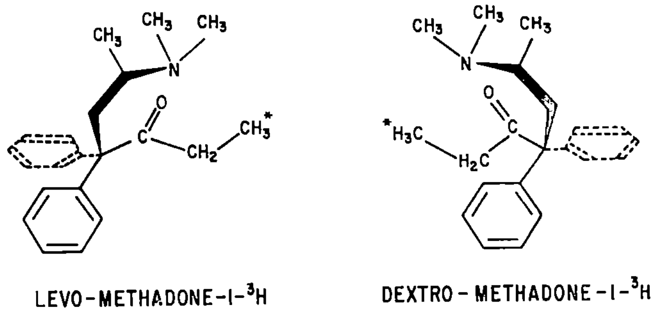

Fig. 1 Optical enantiomorphs of methadone. * Position of radio-label.

Male Wistar rats (110–150 g) were injected subcutaneously with a 10 mg kg^{-1} dose of *d*-methadone-1-^{3}H, approximate specific activity 6 μCi mg^{-1} (New England Nuclear, Boston; radiochemical purity >99%; non-radioactive *d*-methadone carrier prepared as previously described[16]). They were lightly anaesthetized with ether and blood samples collected by intracardiac puncture in heparinized vacutainer tubes at set time intervals and immediately centrifuged for plasma. The brains were removed by decapitation and the concentration of drug in diluted 2 ml. aliquots of plasma or brain homogenates estimated as described for *l*-methadone[14]. The comparative mean values on distribution of dextro and laevo-methadone-1-^{3}H in brain and plasma at different times and half-lives after a single subcutaneous injection are given in Table 1. Comparatively higher levels of *l*-isomer in rat brain were probably due to the higher lipid-solubility of this isomer (partition coefficients of *l*- and *d*-isomer in octanol/buffer, *p*H 7.4, were 57.3 and 28.3, respectively). The

Table 1 Comparative Distribution of Dextro and Laevo-Methadone-1-^{3}H in Rat Brain and Plasma and Half-lives after a 10 mg kg^{-1} (Free Base) Dose by Subcutaneous Injection

	0.5 h	1 h	2 h	6 h	12 h	24 h	48 h	1 week	3 weeks	Half-life* (h)
Laevo-methadone-^{3}H-Brain	3,869	4,502	2,717	855	60	25	27	20	21	2.4
Plasma	1,798	1,400	1,479	645	38	17	—	—	—	3.7
B/P†	2.15	3.21	1.83	1.32	1.58	1.47	—	—	—	--
Dextro-methadone-^{3}H-Brain	3,265	2,069	1,130	110	57	35	44	32	13	1.02
Plasma	536	417	278	43	15	6	3	—	—	1.5
B/P†	6.09	4.96	4.06	2.56	3.80	5.83	14.66	—	—	—

Data represent mean value (ng g^{-1} wet brain weight or ng ml.$^{-1}$ plasma) of two animals for *d*- and four animals for the *l*-isomer at each time period.

* The half-lives were calculated from values on distribution of isomers up to 6 h.

† B/P represents the ratio of mean brain to plasma concentrations.

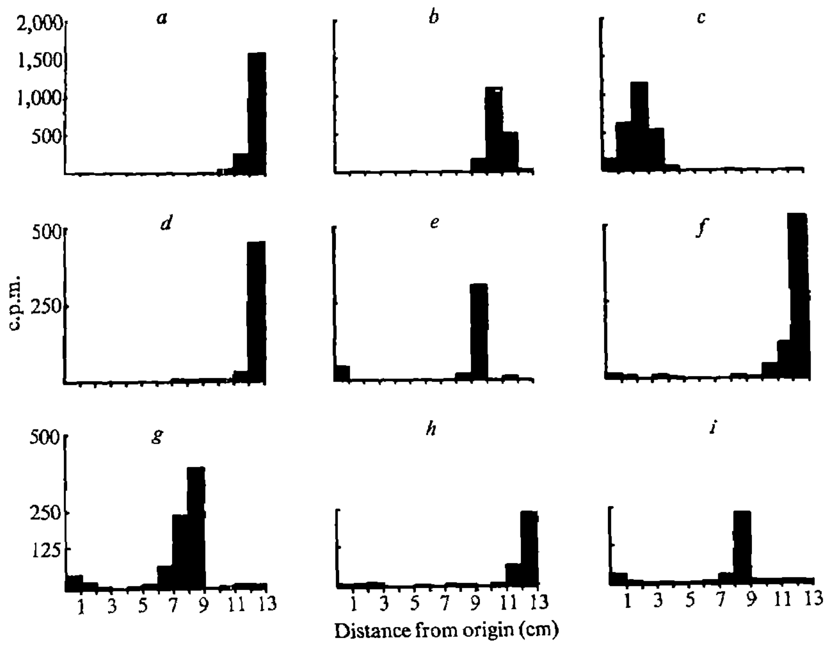

Fig. 2 Radioscans of thin-layer chromatograms (ITLC) of chloroform-isopropanol extract of rat brain 30 min after a 10 mg kg^{-1} subcutaneous injection of *d*-methadone-1-^{3}H. *a*, Silica gel, S_1: ethyl acetate-methanol ammonia (17 : 2 : 1, v/v); *b*, S_2: solvent system: benzene-ethyl acetate-methanol-ammonia (80 : 20 : 1.2 : 0.1, v/v); *c*, ITLC alumina, S_3: benzene-n-butyl ether (19 : 1, v/v); *d*, ITLC, silica gel, residue from 'Amberlite XAD-2' column, 30 min brains, system S_1; *e*, ITLC of *d* with system S_2; *f*, 6 h brains, residue from 'Amberlite XAD-2' column, ITLC, silica gel, system S_1; *g*, ITLC of *f*, system S_2; *h*, 12 h brains, residue from 'Amberlite XAD-2' column, ITLC silica gel, system S_1; *i*, ITLC of *h* with system S_2.

basic procedures for qualitative identification of *d*-methadone-1-^{3}H in groups of four brains removed 0.5, 6 and 12 h after a single subcutaneous 10 mg kg^{-1} injection were similar to that described[14] for *l*-methadone. The radioscans of thin layer chromatograms (Fig. 2) at these time periods showed a single peak of radioactivity due to *d*-methadone-1-^{3}H in different solvent systems. In contrast, *l*-methadone scans[14] consistently showed the presence of a metabolite in the brain in free form at the time of peak analgesia and as a protein-conjugate later in addition to free *l*-methadone. There were also marked differences in biologic half-lives of the isomers in rat brain and plasma at identical doses. Persistence of both free isomers in the rat brain and lack of striking differences in reversible protein binding of two isomers (ultrafiltration technique using 'Centriflo' membrane cones (Amicon Corp.) could account for the fact[17] that the toxic actions and LD_{50}s of these isomers show no configurational discrimination by the intravenous or intraventricular route.

The mean values for free *d*-isomer excreted in rat urine and faeces 96 h following identical 10 mg kg^{-1} subcutaneous doses were 8.29, 7.37%, respectively; total radioactivity, 15.99, 21.01%, respectively. Mean values for free *l*-isomer[16] in urine and faeces were 11.31, 14.78%, respectively; total radioactivity 19.49, 29.8%, respectively.

Chromatography of the pooled filtered urine of rats given 10 mg kg^{-1} subcutaneous injection of *d*-methadone-1-^{3}H on 'Amberlite XAD-2' eluted with methanol-ammonia (300 : 5) gave a residue, which was separated into methanol-soluble and insoluble fractions. The methanol-soluble fraction was further resolved on 'Gelman' ITLC into two subfractions using ethyl acetate-methanol-ammonia (17 : 2 : 1, v/v), polar metabolites, R_F 0.0 amounting to approximately 70% of total excreted urinary radioactivity and nonpolar metabolites, R_F 1.0 (Fig. 3*a*). (In the case of *l*-methadone-1-^{3}H, polar metabolites amounted to 22% of total urinary radioactivity[16].) The nonpolar metabolites eluted from large ITLC sheets were resolved on ITLC using benzene-ethyl acetate-methanol-ammonia (80 : 20 : 1.2 : 0.1, v/v) into 4 metabolites, R_F 0.08, 0.27, 0.58, 0.96 with approximate distribution of radioactivity as 42, 10, 32 and 16%, respectively (Fig. 3*b*). These compounds were separately eluted

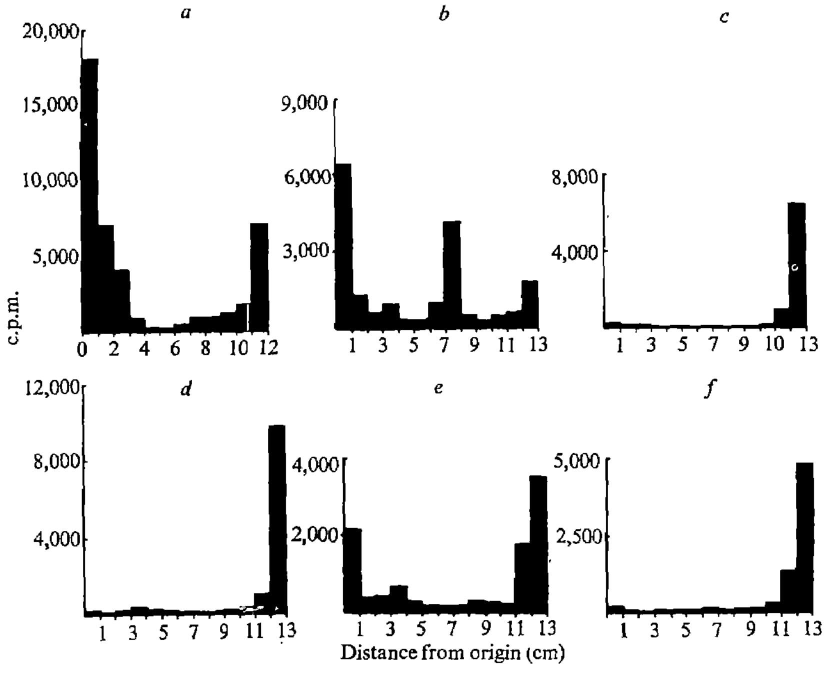

Fig. 3 Radioscans of ITLC from urine of rats given 10 mg kg^{-1} subcutaneous dose of *d*-methadone-1-^{3}H, processed on 'Amberlite XAD-2' resin: *a*, methanol-soluble fraction of residue from 'Amberlite XAD-2' column, with solvent system S_1; *b*, ITLC of subfraction R_F 1.0 of methanol-soluble fraction with system S_2; *c*, ITLC of polar subfraction R_F 0.0 of methanol-soluble fraction after enzymic hydrolysis in system S_1; *d*, ITLC of organic extract of acid-hydrolysate of R_F 0.0 subfraction, system S_1; *e*, ITLC of organic extract from *d* in system S_2; *f*, ITLC of extract from acid-hydrolysed methanol-insoluble residues from 'Amberlite XAD-2' column in system S_1.

with methanol and characterized as *d*-methadone N-oxide (R_F 0.08), 2-ethylidene-1,5-dimethyl-3,3′-diphenyl pyrrolidine (R_F 0.27), *d*-methadone (R_F 0.58) and *p*-hydroxyphenyl derivative of *d*-methadone (R_F 0.96), respectively, by co-chromatography with authentic samples.

The polar fraction (R_F 0.0) proved to be predominantly glucuronide conjugates by enzymic hydrolysis with β-glucuronidase (Fig. 3*c*). Acid-hydrolysis of conjugates and subsequent extraction with chloroform-isopropanol (3:1, v/v) and ITLC with ethyl acetate-methanol-ammonia (17:2:1, v/v) (Fig. 3*d*) and with benzene-ethyl acetate-methanol-ammonia (80:20:1.2:0.1, v/v) (Fig. 3*e*) showed the formation of *p*-hydroxyphenyl *d*-methadone N-oxide (R_F 0.04), *p*-hydroxyphenyl pyrrolidine derivative (R_F 0.27), *d*-methadone (R_F 0.68), and *p*-hydroxyphenyl *d*-methadone (R_F 0.96) with approximate distribution of radioactivity as 25.3, 14.3, 5.7, and 54.7%, respectively (Fig. 3*e*). Acid hydrolysis of the methanol-insoluble residue of the eluate from 'Amberlite XAD-2' column, extraction and ITLC of extract with ethyl acetate-methanol-ammonia (17:2:1, v/v) (Fig. 3*f*) and subsequent resolution with system: benzene-ethyl acetate-methanol-ammonia (80:20:1.2:0.1, v/v) provided a pattern of metabolites identical to that given in Fig. 3*e*.

The major metabolic pathways for *d*-methadone with qualitative similarity to *l*-isomer[15] are: (*a*) *p*-aromatic hydroxylation by hepatic microsomal mixed-function oxidase system which has a low order of substrate specificity, (*b*) glucuronide conjugation, and (*c*) N-oxidation[18]. By contrast with *l*-methadone only minor amounts of pyrrolidine[19,20] and *p*-hydroxyphenyl pyrrolidine metabolites[21] were formed; thus mono-N demethylation and subsequent cyclization are a very minor metabolic route in *d*-methadone. These *in vivo* findings with *d*-methadone are consistent with earlier observations from *in vitro* liver microsomal[22,23] and isomeric substrate studies[24] where the active *l*-isomer was shown to be more readily N-dealkylated than inactive *d*-isomer, and N-dealkylation rather than N-oxidation was shown to be stereoselective.

These observations on comparative metabolism *in vivo* of optical enantiomorphs of methadone-1-^{3}H at identical 10 mg kg^{-1} subcutaneous doses strongly suggest that (1) the stereoselective N-demethylation pathway as previously postulated[14] is a preferential route with active *l*-isomer; (2) significant differences exist in half-lives of isomers in plasma and brain; and (3) the formation of an apparently active metabolite in rat brain occurs with *l*-isomer[14], but not with *d*-isomer.

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Milk Proteins: Reply

We are grateful to Dr Wheelock[1] for drawing our attention to some mistakes in our paper[2]. The α_s-casein was inadvertently labelled α-casein and in error had been included as a glycoprotein, which it is not. This correction, which reduces the percentage of milk proteins which are glycosylated, further emphasizes the wider argument presented in the paper, based on various analyses of which bovine milk is only one, that extracellular proteins do not, of necessity, require glycosylation for export from the cell.

With regard to the other points raised, K-casein referred to in refs. 3 and 4 is the monomeric reduced form, not the native disulphide bridged polymer. Although only 28% of monomeric K-casein is glycosylated[4], the situation concerning the polymer is uncertain. We did not list α-lactalbumin as a glycoprotein because the glycosylated form (the existence of which was stated) accounts for less than 10% of the total α-lactalbumin in bovine milk.

The role of the carbohydrate moiety of K-casein in the interactions of the caseins has not been resolved yet by the workers in this field. Lysozyme, a glycosidase, has a similar coagulation action on casein micelles to that induced by rennin[5], while Talbot and Waugh[6] related the stabilizing capacity of K-casein to the content of one of the carbohydrates, N-acetylneuraminic acid. Even the critic of our paper has expressed the opinion that the rate of action of rennin is influenced by the nature of the saccharide unit[7]. Therefore, on the evidence available the use of K-casein as an example of anti-recognition is not invalid.

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Relation between Glucose Absorption Rate and Serum Globulin Concentration in Man

GLUCOSE absorption rate has been shown to be depressed in patients with acute and chronic systemic bacterial infections[1]. Similarly, the weight of D-xylose excreted after an oral load is decreased in such patients[2], probably also as the result of impaired absorption. The cause of these abnormalities is unknown and they are not due to a change in jejunal morphology. Whether systemic parasitic infestations also lead to an impairment of monosaccharide absorption has not been investigated in man.

Eighteen Zambian African subjects, all in-patients at the University Teaching Hospital, Lusaka, from many Zambian tribes[3], were studied. The purpose of the investigation and the experimental procedure were explained. They had been admitted with a wide variety of diagnoses, but in none was there clinical evidence of an infection, malnutrition or gastro-intestinal disease. Results for glucose absorption rates in thirteen of them have previously been reported[4–6]. Eleven were men and seven women. The mean age was 37 (16–61) years, and mean body weight 55 (43–79) kg. Mean haemoglobin concentration was 12.5 (3.9–17.0) g 100 ml.$^{-1}$. Total serum protein was estimated by a modification of the biuret method[7], and electrophoresis was done using a 'Beckman R-101' microzone cell. All determinations were made in duplicate and standard curves using 'Wellcomtrol' assayed serum 'MR 82' (Wellcome Reagents Ltd, Beckenham, Kent) were constructed. Mean albumin was 3.4 (2.4–4.4) g 100 ml.$^{-1}$. Mean α_1, α_2, β and γ-globulin were 0.3 (0.2–0.4), 0.9 (0.4–1.4), 1.0 (0.8–1.2) and 2.1 (1.4–2.9) g 100 ml.$^{-1}$ respectively; 5 h D-xylose excretion was estimated in four after a 25 g oral load[2], and was 5.2–6.4 (mean 5.7) g. Stool parasites were found in one out of thirteen (hookworm ova). Jejunal biopsy specimens were obtained from three subjects which were normal by dissecting-microscope and routine histological techniques[8]. The technique for measuring glucose absorption rate has been described previously[1,4]. A double-lumen tube was positioned in the proximal jejunum and the tests were performed after a 14–18 h overnight fast. A solution containing 200 mmol l.$^{-1}$ glucose, 100 mmol l.$^{-1}$ sodium chloride, and 0.50 g 100 ml.$^{-1}$ polyethylene glycol 4,000 was pumped at a constant rate of 12.0 ml. min^{-1} through a proximal opening, and intestinal content was collected from a distal opening into the other lumen 30 cm further along the jejunum by siphonage. The mean distance of the proximal opening past the duodeno-jejunal flexure was 15 (1–38) cm. Three 10-min collections of fluid were obtained after an equilibration period of 35 min. Laboratory methods and calculation of absorption rates were as previously described[1,4].

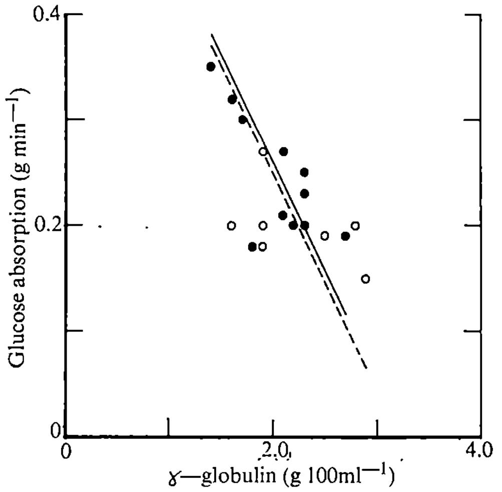

Fig. 1 Correlation between glucose absorption rate (g min^{-1} 30 cm of jejunum^{-1}) and serum γ-globulin concentration (g 100 ml.$^{-1}$). In the subjects in whom the infusions were made at less than 20 cm distal to the duodeno-jejunal flexure (●) the correlation is inversely significant ($P<0.01$); the equation for the calculated regression line (——) is $x=3.25–4.89\ y$. When data from all of the subjects are included in the analysis, the correlation is also inversely significant ($P<0.01$); the equation for the calculated regression line (- - -) is $x=3.23–4.93\ y$.

The mean glucose absorption rate for the eighteen subjects was 0.23 (0.15–0.35) g min^{-1} 30 cm of jejunum^{-1}; the inverse correlation between absorption rate and tube position was significant ($r=-0.51$; $P<0.05$). As well as analysing data from the eighteen subjects together, we considered separately, those obtained when the infusion was made at <20 cm (mean 8 (1–18) cm; $n=11$), and >20 cm (mean 26 (22–38) cm; $n=7$) distal to the duodeno-jejunal flexure. The correlations between individual absorption rates and total and γ-globulin concentrations were inversely significant for all subjects ($r=-0.58$; <0.02, and $r=-0.62$; $P<0.01$), and also for those in whom the infusion was made at <20 cm past the duodeno-jejunal flexure ($r=-0.62$; $P<0.05$ and $r=-0.74$; $P<0.01$). Fig. 1 shows the association between individual absorption rates and serum γ-globulin concentrations. There was no significant correlation between absorption rate and age, body weight, haemoglobin, albumin or α_1, α_2, and β-globulin concentrations. The absorption rates in the subjects who had xylose tests were 0.35, 0.27, 0.27 and 0.15 g min^{-1} 30 cm of jejunum^{-1}. The three subjects who had jejunal biopsy specimens examined had absorption rates of 0.27, 0.27 and 0.15 g min^{-1} 30 cm of jejunum^{-1}.

An inverse association between serum total and γ-globulin concentrations and glucose absorption rate from a 200 mmol l.$^{-1}$ glucose solution has been demonstrated. The cause of the high globulin in some of the subjects, none of whom had clinical evidence of an infection, is unknown. Malaria, schistosomiasis and helminthiasis were probably responsible for most. The present data show that a small rise in γ-globulin concentration can be associated with a marked impairment in absorption rate (Fig. 1). There was no significant association between absorption rate and serum albumin concentration. Falaiye[9] has suggested that hypoalbuminaemia is important in the aetiology of malabsorption in asymptomatic Nigerians. In that study, although improved absorption followed a rise in albumin, the total globulin concentration fell markedly during the period of investigation. Malabsorption of fat and xylose has been demonstrated in some patients with active rheumatoid arthritis[10]. It seems from that and the present study that a high serum globulin concentration in inflammatory and infective disease is associated with an impairment of absorption, even though the jejunum is morphologically normal.

Glucose absorption in Zambian African subjects takes place over a relatively short length of proximal jejunum, and little transfer seems to occur distally (Cook and Snook, unpublished). In the eighteen subjects in the present study there was a significant inverse relation between absorption rate and tube position which, however, did not influence the conclusion.

A previous study has shown a significant correlation between glucose absorption rate from a 30 cm jejunal segment and 5 h D-xylose excretion after a 25 g oral load[1]. It therefore seems possible that there is a significant impairment of monosaccharide absorption from the diet of subjects with chronic infections. Parasitic diseases are extremely common in developing areas of the world. It seems probable that sub-clinical malabsorption is a common sequel.

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Neural Control on the Activity of the Calcium-transport System in Sarcoplasmic Reticulum of Rat Skeletal Muscle

IF the normal nerve supply to a slow skeletal muscle is replaced by a foreign, fast motor innervation, its isometric twitch response is speeded up, to resemble that of a fast muscle[1-4]. In cross-innervated rat soleus, the molecular basis for this transformation has been located to an effect on the molecular properties of myosin. The reduction in twitch contraction-time was found to be associated with coordinate increases of the maximum speed of shortening and of myosin ATPase activity[5,6]. In similar experiments with cat soleus, however, both the maximum contraction velocity and the ATPase activity of isolated myosin were only slightly changed under the experimental conditions[6-8]. Demonstration of an enhanced maximum capacity for accumulation of Ca^{2+} in the isolated sarcoplasmic reticulum from cat reinnervated soleus led to the alternative suggestion that fast innervation to a formerly slow muscle accelerated the time-course of the active state by increasing the rate of translocation of Ca^{2+} from the myofibrils into the lumen of the intact sarcoplasmic reticulum[8,9].

This hypothesis, because of its wider implications concerning a rate-limiting role of intracellular Ca^{2+} passage on the muscular contraction-relaxation cycle, requires two conditions. First, a conditional expression of the activity of the membrane-bound Ca^{2+}-transport system of reticular membranes by fast motor innervation must be more definitely proven; second, that the effect is verified in reinnervated slow muscles from mammalian species other than the cat.

The sciatic nerve of young adult male Wistar rats was severed on one side, and conditions arranged to promote reinnervation of the soleus muscle from the regenerating nerve stump, as described by Miledi and Stefani[4]. The process was completed in three to four months, when the reinnervated muscles had reached an average fresh weight of about 100 mg and about 70% of that of the contralateral, unoperated muscles. The effects of this operative procedure were shown to be similar to those after cross-innervation regarding twitch contraction time of the reinnervated soleus[4].

In our experiments, the paired, operated and contralateral muscles from eight to ten rats were separately pooled and the tissue homogenates, prepared in 0.3 M sucrose, were fractionated by differential centrifugation[10]. Isolation and purification of myosin from the crude myofibrillar sediment was identical to that described previously[10]. In our experiments, the myosin from the reinnervated soleus had a mean ATPase activity of 0.36±0.08 and 1.22±0.21 μmol P_i min^{-1} mg^{-1} protein, with Ca^{2+} and EDTA as the respective activators[10,11], as compared with control values of 0.24±0.05 and 0.86±0.10. The rate of ATP hydrolysis by myosin therefore appeared to be enhanced after changing the nerve supply to the muscle, but did not reach the high values found with purified myosin from the fast muscle, normal extensor digitorum longus (0.69±0-10 and 2.42±0.23 μmol P_i min^{-1} mg^{-1} protein for Ca^{2+}-activated and EDTA-activated ATPase activities, respectively). Sciatectomy and subsequent reinnervation of soleus was less effective in the change of myosin from a "slow" to a "fast" molecular form than cross-innervation, by which an almost complete transformation of myosin has been obtained[5,6].

Table 1 Biochemical Transformation of Isolated Sarcoplasmic Reticulum from Rat Soleus Induced by Foreign Motor Innervation

	Control soleus		Reinnervated soleus
Ca^{2+}-uptake, initial rate	0.10±0.02		0.23±0.03
EGTA-sensitive, Mg^{2+}, K^+ ATPase activity	0.19±0.09	(7)	0.35±0.09
Rotenone-insensitive, NADH-cytochrome c reductase activity	85±9	(6)	86±12

Activities are expressed as μmol of Ca^{2+} accumulated and P_i formed, or nmol of cytochrome c reduced, per min per mg of microsomal protein, and were measured by methods described by Margreth *et al.*[10]. Mean values are reported ± s.e.m. (number of determinations in parentheses) of paired determinations on reinnervated and contralateral muscles. The mean Ca^{2+}-uptake activities of sarcoplasmic reticulum preparations from normally innervated slow soleus and fast-extensor digitorum longus of rats, obtained from the pooled data of these and other experiments were 0.10±0.01 (18) and 0.37±0.05 (7), respectively.

Concomitant changes in the enzymic composition of sarcoplasmic reticulum fragments isolated from soleus were also recorded. The results in Table 1 show that the modifications induced by the foreign innervation to slow muscle were selective to the membrane-bound Ca^{2+}-transport system. The specific activity of the rotenone-insensitive NADH-cytochrome c reductase, electron transport chain was virtually unchanged, and it did not deflect from the relatively high values found in slow as compared with fast muscles[12]. The increased Ca^{2+}-uptake activity of the sarcoplasmic reticulum from reinnervated soleus was due to an effect on the Ca^{2+}-transport system itself, rather than just reflecting an increased Ca^{2+}-accumulating capacity of the microsomal vesicles. Thus the increase concerned the initial rate of Ca^{2+}-accumulation and paralleled that of the Ca^{2+}-transport, EGTA-sensitive ATPase[10] activity.

A phosphorylated protein intermediate was implicated in the ATPase reaction of the sarcoplasmic reticulum, and the extent of phosphorylation of membrane preparations isolated from reinnervated soleus and the contralateral soleus and extensor muscles was assayed[13] using ATP labelled terminally with ^{32}P. The steady-state concentrations of phosphorylated intermediate, expressed as nmol ^{32}P incorporated mg^{-1} protein, were, in the stated order, 0.40, 0.25 and 0.87, in good agreement with the ATPase and Ca^{2+}-uptake measurements. Most of the phosphorylation was due to an increased amount of the ATPase enzyme concerned with Ca^{2+}-transport, which appeared to be supported by results obtained from polyacrylamide-gel electrophoresis[10,14] of the same preparations. The electrophoretic patterns in Fig. 1 show that the relative proportion of a distinct protein species of low mobility currently identified with the ATPase enzyme[10], in the fraction from the reinnervated muscle, was intermediate between that found in the homologous fractions from slow muscle and fast muscle (Fig. 1). In spite of the transformation in protein composition of reticular membranes, corresponding to a slow to fast change, some of the fast-moving electrophoretic components characteristic of the rat soleus microsomes persisted after reinnervation. Conversely they were virtually absent in the homologous fraction from fast extensor[10] (Fig. 1).

We suggest that coupled changes in the isoenzyme composition of myosin, and in the macromolecular composition of reticular membranes, cooperate to the transformation of the twitch characteristics of rat soleus after sciatectomy and the

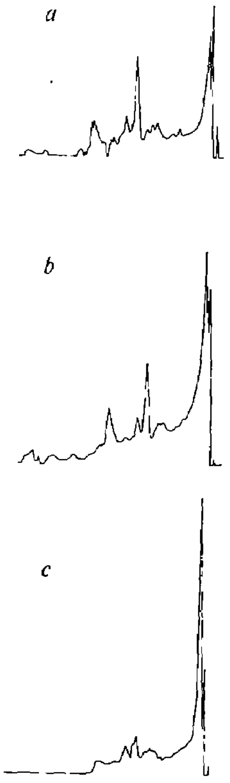

Fig. 1 Polyacrylamide-gel electrophoresis patterns and densitometric records (left side, at reduced scale) of sarcoplasmic reticulum protein from normally innervated, slow soleus (*a*), fast extensor (*c*) muscles and reinnervated soleus (*b*). Gel electrophoresis was carried on about 50 μg of protein, under conditions identical to those described previously[10], by the method of Panet and Selinger[14]. Migration was towards the cathode (3 mA gel^{-1} for 3.5 h). The gels, after staining with 'amido black', were scanned at 620 nm in a 'Gilford recording spectrophotometer'.

subsequent reinnervation from predominantly fast nerve fibres[4]. The concept that the activity of the reticular Ca^{2+}-transport system is specified by epigenetic mechanisms linked to the pattern of impulses from the motor innervation[8,9] to the muscle might be clarified at the molecular level, in terms of a neural control on the synthesis and/or assembly of the transport ATPase into the reticular membranes. The selective accumulation of this catalytic protein in the sarcoplasmic reticulum of rat reinnervated soleus might be equivalent to a permanent derepression, after the loss of a negative feedback control from the original innervation to this muscle, which is supported by acute denervation experiments[10].

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Retention of Pacemaker Activity in Mammalian Myocardial Cells recovered from Liquid Nitrogen

Successful preservation of the mammalian heart in the frozen state is not yet possible because of the sheer bulk of the organ as well as difficulties at the cellular level[1]. Pacemaker activity must be retained, however, and so I have made preliminary studies of sustained rhythmic contractions in dissociated cells. A pacemaker cell in culture is one which, although isolated from contact with neighbours, beats rhythmically[2]. A method for freeze-preservation of sheets of beating rat myocardial cells and myocardial cells frozen in suspension has been described[3], using dimethyl sulphoxide as a cryoprotective agent, in which resumption of contractility was observed on thawing. Estimates of restoration, however, were made on dense populations of cells in confluent sheets, which would be expected to produce a high proportion of beating cells, as myocardial cells capable of pacemaker activity can drive responsive neighbours with which they may come in contact[4].

I report here on the survival of pacemaker activity in isolated mammalian myocardial cells frozen in liquid nitrogen, using ethylene glycol as the cryoprotective agent. A successful penetrating cryoprotective agent must enter the cell freely to avoid producing osmotic dehydration, and it must be non-toxic in the high concentrations necessary to protect against freezing injury[5]. Studies of potential cryoprotective agents have demonstrated toxicity in all but glycerol and ethylene glycol[6,7]. Ethylene glycol can penetrate membranes far more quickly than glycerol[6,9], producing less osmotic stress, so it is the most obvious choice for investigations on the freeze-preservation of mammalian myocardium.

Cultures of foetal rat myocardial cells derived by trypsinization of whole foetal hearts[8] were suspended in growth medium containing 2.5 M ethylene glycol or 2.5 M glycerol or 2.0 M dimethyl sulphoxide. Suspensions containing 10^6 cells ml.$^{-1}$ in 2 ml. glass ampoules were cooled to −196° C at 2° to 3° per min. After storage in liquid nitrogen for 24 h, the ampoules were warmed to 37° C at 200° C per min and the cells placed in growth medium where the cryoprotective agent was diluted to 0.1 M. After 30 min the cells were removed by centrifugation and allowed to settle on glass cover slips. Known volumes of cell suspension were placed over known areas of cover slip, and control cultures were prepared by using equal volumes of unfrozen cell suspension on equal areas of cover slip. Survival was measured 24 h later by counting the total number of isolated cells and the number of isolated beating cells per unit area in the controls, and comparing these with the numbers derived from cultures previously frozen.

The results are shown in Table 1. Ethylene glycol appeared preferable but the recovery of pacemaker activity was low; this may reflect a selective destruction of pacemaker cells, or, perhaps more likely, a failure to resume contractions by some cells which were pacemakers prior to freezing. Cells in suspension may not recover easily from freezing injury because they are still suffering from trypsinization[10,11].

Table 1 Cells Frozen in Suspension

Cryoprotective agent	Surviving intact myocardial cells (% of controls after freezing)	Pacemaker cells (% of total population) Before freezing	After freezing	Calculated % retention of pacemaker activity after freezing
2.5 M ethylene glycol	62±5	30±3	19±6	63
2.5 M glycerol	7±2	28±4	Nil	Nil
2.0 M dimethyl sulphoxide	58±5	23±6	4±2	17

Values are means ± s.e. from five separate experiments.

I studied cells which had attached to cover slips for 40 h prior to freezing and thawing. The same conditions of control applied as before, except that control cultures were passed through medium containing 2.5 M ethylene glycol before reincubation, to allow for cells which became dislodged on handling. Cover slip cultures in 2.5 M ethylene glycol were cooled and warmed at the same rates as before, and survival was measured 24 h after thawing. Table 2 illustrates the improvement in restoration of pacemaker activity.

Table 2 Cells Frozen on Cover Slips

Cryoprotective agent	Surviving intact myocardial cells (% of controls after freezing)	Pacemaker cells (% of total population) Before freezing	After freezing	Calculated % retention of pacemaker activity after freezing
2.5 M ethylene glycol	59±5	39±5	40±3	100

Values are means ± s.e. from four separate experiments.

Cells in suspension survive freezing in dimethylsulphoxide to the same extent as in ethylene glycol. More than 80% of the pacemaker population, however, failed to resume beating after exposure to dimethyl sulphoxide, which probably reflected the toxicity of this compound[6,7]. Glycerol, although nontoxic[6,7], failed to protect myocardial cells to any great extent, probably by its failure to penetrate cells easily and quickly[8,9], so causing lethal osmotic stress.

Cells attached to a surface clearly responded differently to cells frozen in suspension. This may be because they have recovered from trypsinization, in which case they surely provide a more realistic model for studies designed as a prelude to work with whole organs.

The choice of ethylene glycol as a suitable penetrating cryoprotective agent for myocardial cells, based on studies of toxicity and permeability[6-9], has been confirmed. Frog hearts, cooled to −78° C in the presence of multi-molar concentrations of ethylene glycol, resumed spontaneous contractions for a short time when re-warmed[12], and preservation of whole mammalian hearts could in future be attempted using such compounds.

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Cigarette Smoke: Effect of Aqueous and Nonaqueous Fractions on Mitochondrial Function

TOBACCO smoke or components exert inhibitory effects on respiratory cilia[1] and the ciliary activity of *Paramecium*[2-4]. Kennedy and Elliot[5] observed that in *Tetrahymena* tobacco smoke caused structural alteration in the inner mitochondrial membrane followed by the cessation of ciliary activity, attributed to a block in the energy generation process in mitochondria. Because the latter are the primary sites of energy production in an aerobic cell, we studied the effects of tobacco smoke components on mitochondrial function. Effects of aqueous and nonaqueous fractions from whole smoke of tobacco on mitochondrial respiration and coupled energy generation were examined.

Rat liver mitochondria were isolated according to the method of Schneider[6]. Oxygen uptake was measured polarographically by a Clarke-type platinum oxygen electrode. Reaction mixture in a final volume of 3.0 ml., containing mannitol 0.21 M, sucrose 0.07 M, Tris-HCl 0.02 M, EGTA 0.02 mM, P_i 5 mM, and $MgCl_2$ 3 mM (final *p*H 7.2), was saturated with air at 30° C before the addition of oxidizable substrates. To determine the effect of tobacco smoke components, various quantities of the fractions were preincubated for 3 to 5 min in the reaction mixture containing mitochondria (1 mg protein $ml.^{-1}$) before the addition of substrates for O_2 uptake. The State 3 and State 4 respiration rates, respiratory control ratios and ADP:O ratios were obtained by the method of Chance and Williams[7].

Aqueous (W/S) and nonaqueous (W/Ins.) fractions from tobacco smoke were supplied by Dr John Benner and were prepared under standard conditions (35 ml. puff volume, 2 s puff duration and 1 puff per min) by the Core Service Facility of the University of Kentucky Tobacco and Health Research Institute. IRI research cigarettes were smoked with a Heiner-Borgwaldt smoking machine and the fraction of the whole smoke was collected directly in precooled water at 0° C, using a pump on a 'Chemap Vibromixer'. A 5 ml. aliquot of the aqueous solution containing the W/S fraction was evaporated to dryness under vacuum and the dry weight of the residue determined. On the basis of this a 50 mg dry wt residue $ml.^{-1}$ solution of W/S fraction was prepared. The W/Ins. fraction of whole smoke settled on the glass vessel walls and was collected in acetone and evaporated to dryness. The residue was weighed and a 50 mg $ml.^{-1}$ DMSO solution prepared. Comparable volumes of DMSO were added to mitochondrial preparations in control experiments.

Both W/S as well as W/Ins. fractions from tobacco smoke inhibited the State 3 respiration of freshly isolated mammalian mitochondria to varying degrees depending upon the concentration of the fraction and the type of substrate employed (Fig. 1 and Table 1). The W/S fraction also inhibited the State 4 respiration of mitochondria but low concentrations of W/Ins. fraction stimulated it. The O_2 uptake by mitochondria with β-hydroxybutyrate (β-HB), a pyridine nucleotide-linked substrate, was less sensitive to W/S fraction than respiration with succinate. The W/Ins. fraction, on the other hand, inhibited β-HB oxidation more

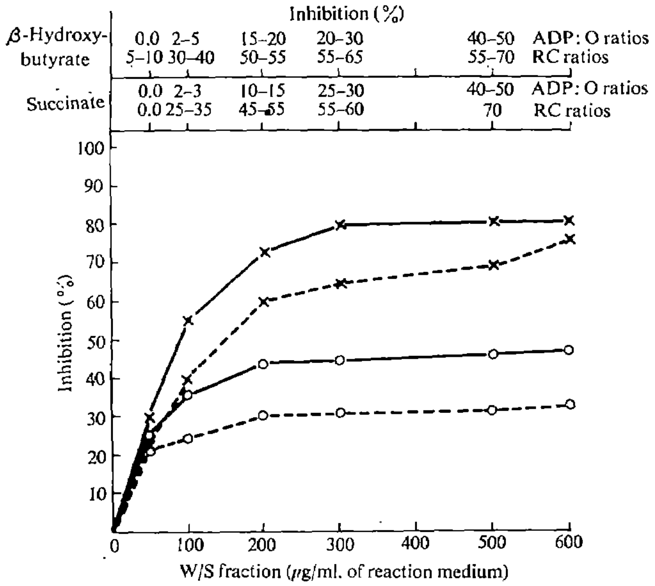

Fig. 1 Effect of aqueous fraction W/S on mitochondrial respiration. W/S fraction from whole smoke of IRI-UK research cigarettes. Oxygen uptake rates recorded after 3–5 min preincubation of rat liver mitochondria in the presence of aqueous fraction. ×——×, Succinate substrate, State 3; ×– – –×, β-hydroxybutyrate substrate, State 3; ○——○, succinate substrate, State 4; ○– – –○, β-hydroxybutyrate substrate, State 4.

than succinate oxidation. Almost complete inhibition of the oxygen uptake occurred in presence of 400–600 μg of W/Ins. residue, but complete inhibition of respiration could not be obtained even in the presence of 1,800 μg of W/S residue.

Respiratory control and ADP:O ratios gradually declined upon treatment of mitochondria with W/S fraction (Fig. 1). In the presence of low concentrations of W/Ins. fraction, respiration control was lost with a simultaneous loss in the ADP:O ratios.

It has been suggested that inhibition of oxygen uptake by lung tissue homogenates and excised lungs on exposure to tobacco smoke is due to inhibition of the mitochondrial system[8]. Our results show that very small amounts of tobacco smoke fractions cause inhibition of mitochondrial respiration. Partial insensitivity (about 20%) of active respiration to high concentrations of W/S fraction (Fig. 1) compared to complete inhibition by W/Ins. fraction (Table 1), and a differential susceptibility of β-HB and succinate oxidation, suggest a different mode of action for the two fractions and a differential sensitivity of mitochondrial respiration with the two substrates. Appreciable stimulation of State 4 respiration by small quantities of W/Ins. fraction indicates the presence of compounds similar to uncoupling agents of mitochondrial oxidative phosphorylation.

Table 1 Effect of Nonaqueous Fraction W/Ins. on Mitochondrial Respiration

Substrate	Conc. (μg ml.$^{-1}$)	State 3 respiration Inhibition %	State 4 respiration Inhibition %	State 4 respiration Stimulation %
Succinate	25	9.0	—	59.0
	50	32.0	—	87.0
	100	63.0	—	47.0
	200	79.0	3.0	—
β-Hydroxy-butyrate	25	29.0	—	13.0
	50	46.0	—	62.0
	100	81.0	12.0	—
	200	97.0	94.0	—

W/Ins. fraction from whole smoke of IRI-UK research cigarettes dissolved in DMSO. Oxygen uptake rates were recorded after 3–5 min preincubation before addition of substrate.

Kennedy and Elliot[5] found the gaseous phase (which is probably equivalent to our W/S fraction) is ciliostatic and caused swelling of mitochondria, but did not disrupt inner mitochondrial membrane. The particulate phase or residue, which is probably equivalent to our W/Ins. fraction, caused a disruption of the inner mitochondrial membrane suggesting a block in energy generation resulting in ciliostasis. Our results show that both fractions cause a decline in energy generation by mitochondria. If ciliostatic activity results from impaired energy generation then both the gaseous as well as the particulate phases of cigarette smoke are involved in ciliostasis due to their ability to inhibit oxidative phosphorylation.

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Changes in Critical Flicker Frequency during and after Fourteen Days of Monocular Deprivation

ALTHOUGH the technique of monocular occlusion has long been used by ophthalmologists[1] in the therapeutic treatment of such conditions as strabismus (squint) and amblyopia, particularly in young children, little experimental work has been directed at determining the nature of visual sensitivity in the nonoccluded eye. Will this eye show a compensatory improvement in acuity as a result of prolonged disuse of the other eye, and, if it does, will this effect dissipate with time following removal of the occluding eye patch? In an attempt to throw some light on this important applied and theoretical problem we have recently conducted a series of studies[2] in which the critical flicker fusion frequency (CFF), a measure of temporal visual acuity, was determined in adult subjects, with normal vision, at periodic intervals during 7 days of monocular deprivation. No significant changes in the CFF of the occluded eye were observed. The temporal pattern of the nonoccluded eye, however, was characterized by an initial decrease in the CFF at 3 and 6 h (that is, poorer acuity), a reversal to the pre-experimental baseline at 9 h, and then a negatively accelerating improvement in performance as a function of monocular deprivation duration. This temporal pattern occurred regardless of whether the dominant or nondominant (weak) eye was occluded. Furthermore, these results were only obtained if a black rather than a white translucent eye patch was used, a finding which indicates that our monocular phenomenon was produced by an absence of visual stimulation *per se* and not by an absence of pattern vision.

In this study, in which the duration of monocular deprivation was extended by 7 days and a 14-day follow-up period was introduced, we wished to determine whether the performance of the nonoccluded eye would continue to improve during the second week or whether it would begin to decline towards the baseline level, an effect which might occur as a result of the subject's adaptation to the novelty of the experimental condition. Contrary to our expectations, we report a "step-like" increment in CFF performance on day 11, an improvement that occurred after a plateau had been reached on days 7 and 9. We also report that this visual improvement is of a long lasting nature, being present to some degree, in most subjects, 14 days after removal of the eye patch.

Sixteen male university students, all with normal vision, were divided into an experimental and a control group, each containing eight subjects. The experimental subjects were required to live for 14 days in a large furnished room (3.66 m x 14.02 m) which contained a radio, a television set, reading material and a variety of games. The subjects were confined to these quarters in groups of four, each subject wearing a black patch over the dominant eye for the entire duration. The CFF, taken only from the nondominant test eye (the nonoccluded eye), was determined before the application of the patch (day 0) and then at intervals of 1, 3, 5, 7, 9, 11 and 14 days of monocular deprivation. Subsequently, the patch was removed and the subjects were allowed to go home. However, they were required to return to the laboratory periodically for follow-up tests, the CFF being taken from the test eye on postocclusion days 1, 3, 5, 7 and 14. Each test session, conducted between 0830 h and 0930 h, was preceded by a meal and 15 min of dark adaptation. During the confinement period, only the test eye was dark adapted since the other eye was already occluded while in the post-confinement period both eyes were dark adapted. These results were then compared with those derived from the corresponding eye (nondominant) of eight non-confined controls who were tested at the same time of the day and at the same time intervals as the experimental group. (A confinement control group was not used since we have already demonstrated that a prolonged period of confinement *per se* does not affect the CFF.)

The stimulus consisted of a white light, at an initial flicker frequency above fusion, which was presented monocularly by a cold cathode modulating lamp mounted at the rear of a standard viewing chamber (Lafayette, model 1202C). The angle subtended by the centrally fixated stimulus was 2°10′, a value assuring full foveal stimulation. The flicker-generating apparatus (Grason–Stadler, model E622) was set at a light-dark ratio of 0.50 and a lamp current reading of 22.6 mA. Eight trials were presented to the nondominant eye at each test period. The descending method of limits was used, the subject's task being to report the first indication of flicker. The arithmetic mean of these eight trials was taken as the descending monocular CFF threshold.

As Fig. 1*a* shows, there was a negatively accelerating improvement in the CFF of the nonoccluded eye up to day 7, a plateau from days 7 to 9, a "step-like" improvement at day 11, and, finally, after the removal of the eye patch, a gradual decline towards the pre-experimental baseline. On the other hand, the CFF of the corresponding eye of the control group showed no systematic changes during the entire 28-day test period. An analysis of variance (mixed design for repeated measures[3]) revealed a significant difference between the two groups ($F=6.49$; $P<0.02$), a significant change over days ($F=10.42$; $P<0.001$), and a significant interaction effect ($F=9.63$; $P<0.001$). Subsequently, a series of individual two-tailed t tests were performed comparing the relative performance of the two groups at the various test periods. This analysis revealed a significant difference at all test periods (P values <0.01), except at day 0, during the 14-day occlusion period. In addition, the increment from days 9 to 11, relative to the plateau from days 7 to 9, was also statistically significant ($P<0.01$).

The results of the follow-up tests indicated the presence of significant after-effects on postocclusion days 1 and 3 (P values$=0.05$) but not on the subsequent days. In spite of this statistical finding, it is important to note that six of the eight subjects, all of whom showed a gradual decline in performance, still had not reached their individual baseline level on day 14, a finding which suggests that these after-effects are long lasting and may persist for a period equal to that of the monocular deprivation duration.

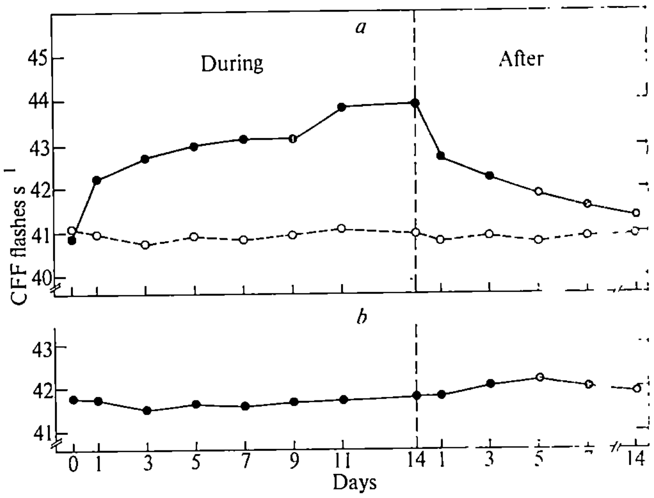

Fig. 1 *a*, Changes in the mean CFF of the nonoccluded eye (●) of the experimental subjects during and after 14 days of monocular deprivation, relative to the changes in the corresponding eye of the control subjects (○). *b*, Changes in the mean CFF of the occluded eye (●) during and after 14 days of monocular deprivation. The increased CFF on postocclusion days 3, 5 and 7 resulted from the aberrant performance of one subject. The baseline difference between the two studies on day 0 is due to the fact that the dominant eye, tested in the second experiment, normally yields a slightly higher CFF value than does the nondominant eye. This difference on day 0, however, was not statistically significant.

In a second experiment the CFF of the occluded eye (dominant) in eight additional subjects was measured during and after 14 days of monocular deprivation, particularly to determine whether a compensatory depression of the CFF might occur between days 11 and 14, the interval which displays the "step-like" improvement in performance of the nonoccluded eye. The procedure was similar to that used with the previous experimental group except that the occluded eye was now tested. The results (Fig. 1*b*) show no systematic changes in the CFF either during the 14-day deprivation period or in the subsequent follow-up period.

The results of this study, together with those we obtained earlier[2], indicate that when one eye is exposed to a prolonged period of darkness the performance of the other eye shows a complex temporal pattern consisting of three components or "limbs": an initial depression of the CFF occurring several hours after occlusion, followed by two periods of enhancement or improvement of the CFF—the first up to day 7 and the second after day 9. In an attempt to provide an explanation of this unusual and long lasting visual phenomenon, we have suggested[2] that it might be placed in the same category as the supersensitivity effects which are known to occur in the higher neural centres after either drug-induced or surgically induced partial deafferentation at the lower levels of the central nervous system, a class of compensatory phenomena which Sharpless[4], in a recent revision of the law of denervation[5], has stated result from prolonged disuse of neural pathways. Although our results reported here seem to be consistent with Sharpless's hypothesis, one important question which remains unanswered is the nature of the mechanisms responsible for producing the three components in the CFF performance curve. To provide an answer, it might be fruitful to obtain electrophysiological recordings from various levels of the visual system of the cat or monkey during and after prolonged non-surgical occlusion of one eye and the presentation of appropriate visual stimuli to both the nonoccluded and occluded eye. Only this type of parallel study may be able to throw some light on the specific mechanisms underlying this unusual interocular phenomenon.

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Hydromechanics of Fish Schooling

VARIOUS explanations for fish schooling have been put forward[1], including the rate of predation[2,3], social[4] and genetic[1] factors. Hydrodynamical effects appear to be important to obligate schooling species. They commonly show migratory movements[4], and the schools usually consist of individuals of the same size range[6,7] (with similar cruising speeds, as these depend on body-length) swimming in synchronization and in regular arrays[8]. The endurance of the fish is found to be increased twice to six times when in schools[16]. These factors may have practical significance, as many commercially important species are found in schools and knowledge of their possible speed and stamina can help design efficient fishing gear.

Breder[5] mentioned some hydrodynamical effects, but presented no analysis of the advantages of swimming closely together in a synchronized manner, which is one of the definitions of schooling[4]. Belyayev and Zuyev[16] have suggested that wake interactions of closely situated fish may reduce the hydrodynamic resistance of individuals in the school, and have experimental results[17] to support their hypothesis. This and other hydromechanical advantages of the close aggregation of swimming fish are examined here. A very large school will appear boundless to a fish swimming inside. I have examined the effects of surrounding fish on a typical test individual in a school moving at constant velocity (including migratory movements and keeping position in currents).

Single fish swimming in shallow waters shed a two dimensional thrust-type[9-11] trail of vortices of alternating sign (Fig. 1). A shallow basin of water is hydrodynamically equivalent to one horizontal layer of the fish school, which can be treated as a two dimensional situation. (Detailed analysis and discussion of quantitative results are in preparation.)

The vortex trail shed by fish *A* (Fig. 1) induces a water velocity relative to the vortices, which is opposite to the swimming direction immediately behind the fish, and in the direction of swimming outside the vortex street. A fish situated directly behind *A* would experience a higher relative velocity and would have to exert extra energy. In position *B*, however, a smaller effort is required and may even be less than that of a solitary fish swimming at the same speed. The best position has been calculated to be midway (laterally) between two fish of the preceding row. Reductions in relative speed of up to 30% were obtained between the best and worst lateral positions of fish *B*. As the thrust (which is equal to the drag for steady swimming) is proportional to the square of the velocity, there are advantages in swimming in a diamond pattern (Fig. 1). In this formation, when the lateral distance between adjacent fish is twice the width of the vortex trail, wakes from two successive lateral rows of fish are cancelled. The third row will encounter a uniform flow and the total energy saving to the school is half the relative gain to the second row. The situation is similar but more complicated for other ratios of lateral distance to trail width.

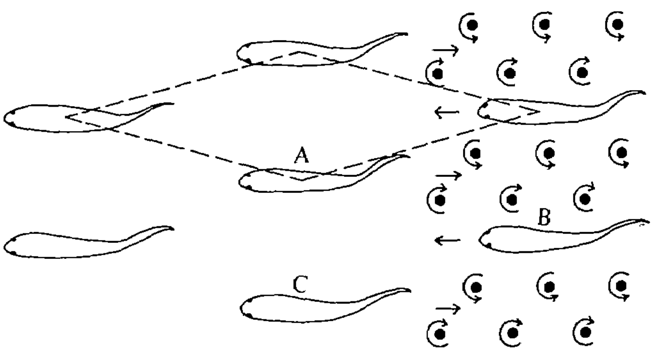

Fig. 1 Part of a horizontal layer of fish in a school, from above. Arrows near vortex streets show direction of induced flow relative to the vortices. The dotted line shows a "diamond" pattern.

Belyayev and Zuyev[16] suggested a configuration similar to that of fishes *A* and *C* in Fig. 1, but interpreted this only as a mechanism for obtaining "neutral" rows of vortices (that is, producing neither thrust nor drag) by expansion of the lateral distance between vortices. It has been shown[12] that the lateral spacing of vortex "streets" is stable for all spacing ratios when parallel "streets" are as close as those found in fish schools. My suggestion seems more reasonable as it also explains the "diamond" pattern actually found[14].

The velocities induced on neighbouring fish to the sides and front are negligible because the velocity field of a potential vortex is proportional to the inverse of the distance from the vortex. The force produced by each fish, however, is influenced by the presence of the neighbours in the same lateral row. This configuration may be compared to a single fish swimming in a rectangular vertical channel, whose dimensions are the distances between two adjacent fish centre-lines, laterally and vertically. Rosenhead[12] has shown that the drag of a body shedding a vortex trail in a confined stream is enhanced by the presence of the barriers. Modified, this can also be shown to be the case for thrust due to oscillatory movements of the fish. This results in another hydromechanical advantage of close aggregation. The thrust of each individual fish may be increased by tens of percentages, without any change in the propulsive cycle and energy expenditure. This factor is dependent on the distance between fish, as the relevant term in the expression for the force[12] is proportional to an integral of the square of the induced velocity. These contributions effectively disappear when the lateral distance between fish is more than one length apart.

I finally considered the effects of neighbouring fish above and below my test specimen. Many obligate schooling species are slender[4] (the length is greater than any other dimension). Newman's[13] analysis of lateral motions of slender bodies in channels is applicable, by representing the surrounding fish by streamline "walls". This requires that fish of successive horizontal layers are directly underneath each other. The forces produced by a given motion may be increased as much as 15% when the vertical distance between fish centre-lines is twice the cross-sectional depth, and 30% when this distance is only 1.5 times the fish depth[13]. This analysis applies also to a one-layer school moving in shallow waters.

These arguments show that hydromechanical factors can play an important role in schooling behaviour of aquatic species. Although this characteristic may have originated for other reasons, significant advantages may be obtained by proper synchronization of movements and correct regular positioning of individuals. The highly nonlinear dependence of all three factors mentioned on the inter-fish distance results in any irregular spacing being wasteful.

The mechanisms of hydromechanical interaction suggested here are highly idealized due to the inviscid flow model, the reduction to two dimensional analysis and the requirement of perfect synchronization of movement. In actual fish schools these effects would probably be smaller as these requirements would be only partially fulfilled. In a calculation, for example, assuming that laterally neighbouring individuals swim in antiphase (when fish *A* is curved to the right, fish *C* deflects to the left), the effect of the first two mechanisms was reduced by an order of magnitude for this case. Also there is cross-coupling between the effects. The lateral influence decreases the shed vorticity required for moving at a given speed, so that the change in induced velocity (streamwise effects), which is proportional to the vortex strength, is decreased.

Hydrodynamical factors may even explain the inclusion of individuals of up to 50% length difference in certain schools[7]. Otherwise, this would imply that the smaller fish would have to swim at much higher speeds than the usual cruising speed of 3 fish-lengths per second[1]. Experimental data[5,8] show regular formations; when fish were swimming the diamond pattern[14] occurred, but disappeared when they stopped. Measured distances between adjacent fish[15,17] are of the right magnitude for the suggested hydrodynamical interactions. Additional data, especially of fast swimming large three dimensional schools with accurate estimates of inter-fish spacings in all directions and sustained cruising speed, are required to determine to what extent the mechanisms described here are actually utilized.

This work was supported by the Science Research Council. I thank Sir James Lighthill for discussions.

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Phytotoxicity of a UHF Electromagnetic Field

It is known that ultra-high frequency (UHF) fields are selectively toxic to plants and seeds[1], but the reasons for this have not been investigated. We have studied the way in which the toxicity of a UHF field is related to various parameters of seeds by observing the effect of the radiation on germination.

We exposed seeds to a 2,450±20 MHz field generated in a Litton cavity chamber by a magnetron of nominal power output 600 W. The samples were placed on a glass shelf 1.5 cm above the floor of the chamber, and we found that the intensity of the radiation was such that a 50 ml. sample of water exposed for 60 s absorbed 270 J g^{-1}.

We exposed dry seeds in glass Petri dishes so that they absorbed 270 J g^{-1}. Before and after treatment the seeds were kept at a temperature of 32° C in the daytime and 29° C at night, at a relative humidity of 75%. The light intensity was 1,500 foot-candles and the length of the day was 15 h. Seeds were considered to have germinated if after five days the radicle extended 3 mm, and germination levels were expressed as the proportion which germinated compared with the untreated controls. Each experiment was repeated ten times with ten seeds of several species used each time.

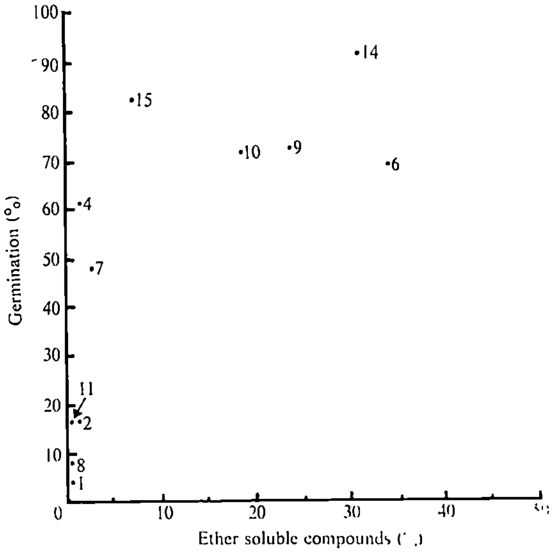

Fig. 1 Relation of susceptibility to a 2,450±20 MHz field (271 J g^{-1}) to ether soluble extract of several species. Key to species numbers: 1, Jackbean (*Canavalia ensiformis*); 2, corn (*Zea mays*); 3, bush bean (*Phaseolus linensis* var. Henderson bush); 4, sorghum (*Sorghum vulgare*); 5, pigweed (*Amaranthus* spp.); 6, cucumber (*Cucumis sativus*); 7, Honey mesquite (*Prosopis juliflora*); 8, lima bean (*Phaseolus linensis* var. Fordhook 242); 9, cotton (*Gossypium hirsutum*); 10, soybean (*Glycine max*); 11, black bean (*Stizolobium deeringiamum*); 12, curled dock (*Rumex crispus*); 13, jungle rice (*Echinochloa colonum*); 14, mustard (*Brassica* spp.); 15, wheat (*Triticum vulgare*).

We examined the susceptibility of seeds to the radiation as a function of the mass per seed, the volume per seed, the density of the seeds, the moisture content of the seeds, their specific heat and chemical constituents, and the amount of energy absorbed. Mass was determined for a number of seeds, and volume by observing the displacement when seeds were added to water (before significant absorption took place). Seeds dried at 40° C to a moisture content of approximately 7% were soaked in water for varying periods of time, removed from the water, blotted until the external surface was dry, and exposed to 32 J g^{-1} radiation. Moisture content was then compared to relative susceptibility. The specific heat was measured using standard calorimetric methods[2].

Seed moisture content can affect specific heat values; the variation was between 9% and 13%. We expect that long-chained polymers or other large molecules present good targets for electromagnetic radiation. Proteins, nucleic acids, fatty acids, starches and sugars are present in plant cells in substantial amounts.

We determined total protein gravimetrically after extraction with 0.1 M and precipitation with 5% trichloroacetic acid[3]; total nucleic acids were determined using the procedures of Click and Hackett[4]. Ether solubles were determined gravimetrically and soluble sugars and hydrolysable starches spectrophotometrically[3]. The data were then correlated with relative susceptibilities of the species to the UHF field using a least squares fit to a straight line. Linear correlation coefficients were calculated and tested by computing the probability of attaining the experimental coefficient from uncorrelated data.

Measurements having a linear correlation coefficient greater than 0.5 and probabilities of 10% or less of accidental correlation in 15 species examined (Table 1) were mass per seed, volume per seed, ether solubles, energy absorbed from the

Table 1 Seed Properties with Significant Linear Correlation Coefficients

Characteristic	Linear* correlation coefficient	$a \pm \sigma_a$	Probability† (%)	$b \pm \sigma_l$	Number of data points
Mass/seed	0.62	57.1± 8.1	2	−47.7 ±16.67	15
Volume/seed	0.75	61.9± 6.9	0.1	−70.3 ±17.30	15
Density	0.29	99.3±49.5	35.0	−44.5 ±41.1	15
Protein (%)	0.42	67.5±14.7	20.0	−3.19 ± 2.43	10
Soluble carbohydrate (%)	0.50	69.5±15.1	15.0	−0.618± 0.360	11
Nucleic acids µg/gf wt	0.09	55.0±12.5	<50.0	−0.033± 0.137	9
Ether solubles (%)	0.72	27.4± 9.8	1.0	1.89 ± 0.61	11
Specific heat	0.13	30.6±44.9	<50.0	22.1 ±61.7	10
Absorbed energy/20 g	0.54	150.7±57.9	10.0	−0.029± 0.16	10
Energy absorbed/seed	0.76	62.8± 8.7	1.0	−0.26 ± 0.08	10
Log (energy absorbed/seed)	0.91	97.8±10.6	<1.0	−17.5 ± 2.9	
Water content					
Wheat	0.77	70.5±19.2	2.0	−2.69 ± 0.92	8
Sorghum	0.77	117.3±21.5	2.0	−3.27 ± 1.09	8
Mesquite	0.96	119.7± 9.4	0.1	−1.87 ± 0.22	8
Cotton	0.80	115.7±10.3	1.8	−1.26 ± 0.39	8
Corn	0.73	115.9± 9.9	3.0	−1.62 ± 0.62	8
Dicots.	0.65	123.7± 7.4	0.1	−1.84 ± 0.21	24
Monocots.	0.92	126.6±18.9	0.1	−4.01 ± 0.99	16

* The sign of the linear correlation coefficient is the same as that of *b*, but only the absolute magnitude is important in our analysis.
† Probability in % that an uncorrelated distribution would give the same results.

field per 20 g of seed sample, energy absorbed per seed, and imbibition moisture content.

Fig. 1 shows a strong correlation of susceptibility to ether soluble compounds (0.72). This might result from some insulating effect of lipoidal material against the field (non-polar substances have a low dielectric constant), or from the decline of a component associated with susceptibility as lipoidal substances increased.

Both specific mass (Fig. 2) and specific volume are strongly related to susceptibility. This strong relationship might be due to the presence of increasing amounts of a component molecule associated with susceptibility in the larger seeds or to volume/surface relationship. It seems that seed density has little influence on susceptibility (Table 1). We cannot explain why large seeds are more susceptible than closely packed small seeds of an equal mass.

UHF fields produce both thermal[5,6] and non-thermal effects[6,7] in biological material. At the field intensities used here, it is not possible to distinguish between thermal and non-thermal effects (Fig. 2). If the correlations between increasing water content and susceptibility (Table 1) are entirely due to the physical nature of water in an electromagnetic field, it should be possible to calculate a linear function that will describe susceptibility of all species as the water content is increased. In two of five species, it seems that linear function is possible while in three species the function is non-linear (Fig. 3). Thus, increasing susceptibility in response to increasing water content does not necessarily follow a linear mathematical relationship. This indicates that the response is mediated by biological factors, for example, internal structure, other molecules which absorb from the field or act as insulators to it, the inherent resistance of cells of a given species to excessive thermal energy, or other unknown factors.

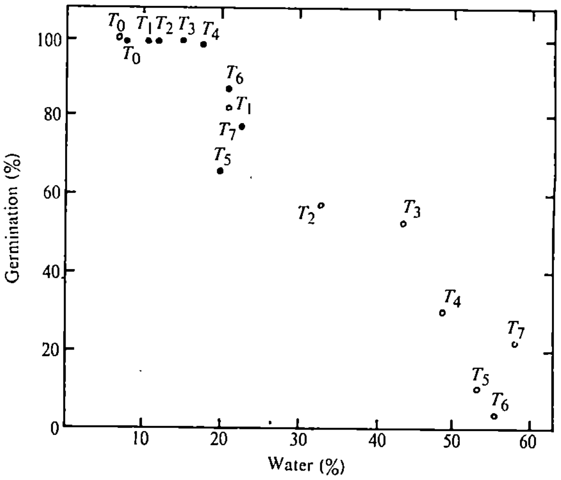

Fig. 3 Imbibition moisture content of seeds as related to susceptibility to a 2,450±20 MHz field in corn (○) and mesquite (●). Key to exposure time codes: T_0, field (32 J g^{-1}) applied immediately; T_1, field applied after 15 min imbibition of moisture; T_2, T_3, T_4, T_5, T_6, T_7, field applied after 30, 45, 60, 120, 180, and 240 min respectively.

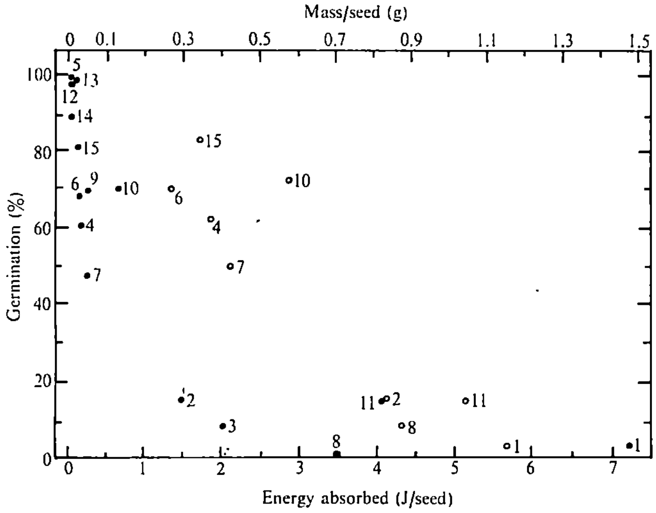

Fig. 2 Relation of susceptibility to a 2,450±20 MHz field (271 J g^{-1}) to mass per seed and energy absorbed per seed for several species. Species numbers as in Fig. 1. ●, Data for mass per seed; ○, data for energy per seed.

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BOOK REVIEWS

Popper's Third World

Objective Knowledge : an Evolutionary Approach. By Karl R. Popper. Pp. x+380. (Clarendon: Oxford; Oxford University: London, November 1972.) £4.50 cloth; £1.50 paper.

FROM time to time one still meets people who have not yet read Popper's *The Open Society and its Enemies.* My own reaction is to envy them the deeply rewarding intellectual experience they still have ahead of them. *Objective Knowledge* is philosophical in a more austerely technical sense of the word, and it will not mean very much to those who are bored by or contemptuous of the discussion of problems which Descartes, Locke, Hume and Kant considered worthy of deep and anxious thought.

Although Popper is a commensense realist, he dismisses as a subjectivist blunder the commonsense theory of knowledge, according to which knowledge is a specially secure kind of belief and scientific knowledge a specially secure kind of knowledge.

Like Kant, Popper builds anew among the ruins left by David Hume's frightening disclosure that our "knowledge" is not only the nature of belief but of rationally indefensible belief—of an irrational faith. Of this disclosure, as Popper reminds us, Bertrand Russell had already said, perhaps a little too strongly: "The growth of unreason throughout the nineteenth century and what has passed of the twentieth is a natural sequel to Hume's destruction of empiricism."

We are left then with the problem of which "induction" professed to be the solution—the problem of how we come to formulate more or less trustworthy scientific generalizations based upon the evidence of the senses. Popper believes he has solved this problem and his solution as it was propounded in *The Logic of Scientific Discovery and Conjectures and Refutations* is now very widely accepted.

The traditional answer to the problem of how scientific discoveries come to be made has been "by induction". Inductionism is a complex of ill-defined attitudes of thought that defy summarization, but right at the heart of it lies the belief that there exists a calculus of discovery—a formulary of intellectual behaviour by strict obedience to which we may be led to the formulation of reliable truths concerning the nature of the world around us. Popper has no use for induction; nor had the early Bertrand Russell who wrote (1903): "What is called induction appears to me to be either disguised deduction or a mere method of making plausible guesses."

In Popper's view scientific knowledge is essentially hypothetical in character and scientific laws arise as imaginative conjectures about what the truth might be. The hypotheses in which we come to have the greatest confidence are those which have stood up to the repeated assaults of critical appraisal. From time to time empirical evidence makes it possible to eliminate a hypothesis and thus to discriminate between one hypothesis and another; yet no hypothesis is ever so securely established as to be altogether beyond the reach of criticism and, if need be, of reformulation. This is the great lesson that Popper drew from Einstein's reconsideration of Newtonian principles, which had come to be regarded by most philosophers and scientists as being of virtually apodeictic certainty. Popper has never maintained, as some parodies of his views suggest, that Einstein was right and Newton was wrong—indeed this kind of black and white formulation has no place in Popper's scheme of thought.

If we regard the implications of a hypothesis as its logical "output" then the Popper scheme can be seen to import into methodology the ubiquitous notion of "negative feedback", that is the control of performance by the consequences of the act performed. Another interesting parallel which deserves a fuller treatment than Popper had had time to give it here is the parallel between Darwinian evolution and the autochthonous origin of scientific ideas (compare the autochthonous origin of genetic information)—of scientific ideas which struggle for their continued existence in the face of repeated criticism and of which only the fittest survive to form the body of received scientific opinion.

Popper has a very good feeling for the conduct of science at bench or shop floor level. For example he says, what all experimental scientists know, that the hypothesis which gives the greatest pleasure when it stands up to criticism is the "risky" hypothesis—the hypothesis that could so very easily have been wrong.

Popper's views are strongly objected to by those who think that the word "hypothetical" is pejorative in character and by methodologists of science who feel diminished by the imputation that they have no inductive method to teach.

The freshest and most original part of Popper's new book is his notion that human beings inhabit or interact with three ontologically quite distinct worlds: world 1 is the ordinary physical world or the world of physical states; world 2, the mental world or world of mental states; world 3 is the world of actual or possible objects of thought; the world of concepts, ideas, theories, theorems and explanations generally, always considered—as we do consider them—objectively, for we do indeed contemplate, discuss, tinker with and propagate these objects of thought. The very imagery we use in discussing world 3 reveals its objective existence outside ourselves, for we "see" an argument, "grasp" an idea, and "handle" numbers expertly or inexpertly as the case may be. The existence of world 3, inseparably bound up with human language, is perhaps the most distinctively human of all our endowments: "I suggest that it is possible to accept the autonomy of the third world and at the same time to admit that the third world originated as a product of human activity. . . ." The third world is not a fiction but exists "in reality". The third world, it may be said, is the greater and more important part of human inheritance; for it is that world which is propagated from generation to generation by tradition, precept, example and deliberate instruction—by those non-genetical processes of heredity to which Waddington, Huxley and I have often called attention.

Popper writes very skilfully and reasons strongly. Those who are determined not to be persuaded by him had best not read him. Others will find his book a very notable addition to the furniture of world 3.

PETER MEDAWAR

Practical Calculation

Numerical Computation. By P. W. Williams. Pp. viii+191. (Thomas Nelson and Sons: London, October 1972.) £2.50 paper ; £5 cloth.

THIS book has material on computer calculations, non-linear, polynomial, linear simultaneous, and ordinary differential equations, finite differences, curve fitting, numerical integration, and eigensolutions. Each chapter has worked examples, some exercises with answers at the end of the book, and bibliographical notes and references.

The book is not meant to be a mathematical text but a guide to good numerical practice; a sound idea, but difficult to achieve. Such a book must be modest in size, and one therefore wonders (*a*) why the first chapter includes Taylor's series, iteration, convergence acceleration, over-relaxation methods and Aitken's Δ^2 process, (*b*) why a chapter on polynomials which appear explicitly very rarely in practice, (*c*) why nothing on ordinary differential equations of boundary-value type, and (*d*) what principle governed the choice of material for which proofs are or are not given.

Most of the selected material is quite good, and the bibliographical notes are very good. But there are serious exceptions. First, one is irritated by many misprints, a page of numbers with no description, unexplained references to other material, and statements such as "If the Gauss-Seidel method fails to converge then the alternative Jacobi method is available".

More important, there are serious errors of fact and principle. These include incorrect statements on Richardson extrapolation, the need for partial pivoting, the partial instability of the Runge-Kutta method, weak instability, Richardson extrapolation with Simpson's rule, and a catastrophic example 4 on page 158 where the printed numbers are quite wrong and the conclusions quite dangerously fallacious.

I can therefore recommend this book only to those who can study it with the support of expert tuition. The rest should wait, hopefully, for a corrected second edition which could, indeed, be a useful addition to the literature.

L. FOX

Science of Synapses

Structure and Function of Synapses. Edited by George D. Pappas and Dominick P. Purpura. Pp. 308. (Raven: New York. Distributed in the Eastern Hemisphere by North - Holland, Amsterdam, 1972.) Hfl. 75; $23.50.

Pappas and Purpura on behalf of the New York Society of Electron Microscopists are to be congratulated on the assembly of an authority of authors to write on anatomical, biochemical and physiological aspects of synapses. The book production is good and is marketed reasonably promptly in that the bibliographies include references to the literature of 1970. One may, as is conventional with reviewers today, reflect that the price makes it expensive for students. But it is sturdily built so that it should survive the abuses of the heavy use of the readership of general and departmental libraries.

Each of the twelve articles is by one or more authors distinguished in their special fields; Pappas, Akert, Bodian and Reese on the structure of synapses; Auerbach, Hall, Gerschenfeld and Whittaker on the biochemistry of synaptic transmission; Kandel on the functioning of *Aplysia* central nervous system; Bennett comparing electrical and chemical synaptic transmission; Purpura on the synaptic organization of the mammalian brain and Broom on the development of synapses—is a list of some of the contributors. The student to whom the preface directs this volume can obtain clear and generally balanced summaries of many of the currently active approaches to synaptic functioning. If an undergraduate, the student will need to be an able one because all the articles do deal with their subject in some detail. And in practice, the book is likely to be of most use to postgraduates and research workers in other aspects of the nervous system who want to know current work on synaptic mechanisms but are exhausted by the sight of piles of titles culled from *Current Contents* that yet remain unread.

A reviewer is supposed to criticize, preferably creatively, although in fact the species in general tends to prey on sins of omission and commission. Personally I do not feel like doing this because I find all the articles very worthwhile however much I might sometimes want to give alternative interpretations and emphasis to those problems discussed in this book which I think I understand. But there is one general problem with which books of this kind and most books published on the nervous system these days do not deal. That is the problem of providing general statements and syntheses of how far we have got in understanding the principles by which nervous systems as a whole work. In fact, a beginner in neural studies may well be put off because she (or he) is likely to find few coherent descriptions of the woods, so full are we with information about the trees. At present mechanisms of neural action have to be studied in this "reductionist" way and it is true, as the preface states, that little can be said about, for example, the mechanisms of memory and behaviour. Yet somewhere along the line "the student" does not need to be put in contact with "the larger picture" if he is to grasp the general importance of the very good work in this kind of collection. Few of us (lacking the confidence and ability of, say, a Sherrington) want, perhaps quite rightly, to write such general articles. Perhaps then a university teacher, uncertain of his role as a projector of facts in this decade of an "explosion of knowledge", can console himself and inspire his audience with enthusiasm by giving a context to the most useful summaries provided by this book.

B. B. BOYCOTT

Ebullient Spectroscopy

Handbook of Commercial Scientific Instruments. Vol. I: *Atomic Absorption.* By Claude Veillon. Pp. xv+174. (Marcel Dekker: New York, September 1972.) $11.75.

THE purpose of this series is to provide a guide to the purchaser of analytical instrumentation from amongst the many domestic and foreign products sold in the USA. This first volume deals with atomic absorption and surveys seventeen manufacturers' atomic absorption instruments model by model. Its aim is to present a guide to intending purchasers by providing specifications, descriptions, schematic drawings, photographs, details of accessories, approximate prices and so forth. The preface states that all of the information presented is based on material supplied by the manufacturers or their representatives. Subsequently it states that the views and opinions expressed are those of the author alone and no responsibility is accepted for their accuracy by the editor, publisher or instrument manufacturer (or their representatives). Since the author is an editor, this is somewhat confusing.

The author has, however, most certainly provided a valuable survey for intending purchasers. The introduction stresses the important features of various functions of AA instrumentation and explains much of the technical jargon that is bandied about by manufacturers. Whilst these may be elementary to a spectroscopist they might well be incomprehensible to (say) a biologist needing to buy an AA instrument to study mercury concentrations in lichens or fungi. Ignoring the edited commercial specifications and accounts in the main section of the text, one goes on to the summary provided by the author at the end. Here there are many valuable expressions of opinion and discussions of "pros and cons" of prisms against gratings, meter against digital read-out, single against double beam facility and so on. The author groups instrumentation into categories according to price range, versatility, and so on, and narrows down the field to a fairly simple choice according to the purchaser's budget and requirements. This section has very considerable merit though one cannot but reflect that its value may be rather transient since instruments become obsolete so quickly, and of course the prices can only be regarded as very approximate.

One of the most interesting features is the author's first assessment of the flame emission technique in the second paragraph of the preface and the caveat introduced in the penultimate paragraph of the final section of the book largely due to the strenuous "emission" lobbying of Professor Fassel's group at Iowa State University. It is true to a limited extent that the higher monochromator cost of a good emission instrument is partly offset by the cost of hollow cathode lamps for atomic absorption. But the view expressed that a high-capability emission instrument can easily perform AA is only true when that "expensive" instrument is further provided with the necessary "expensive" power supply and, of course, "expensive" hollow cathode lamps. Emission in flames is certainly a valuable and indispensable technique for trace analysis of elements such as the alkali metals and several others but good emission instrumentation is more complicated to use and it is very doubtful now if it will ever seriously challenge its younger atomic absorption sister for the generality of trace metals analysis. Radio frequency plasma emission methods show a little more promise, but the multielement capability, simplicity and sensitivity of non-dispersive atomic fluorescence spectroscopy are much more likely to offer most challenge to atomic absorption.

This is a useful book but it may become very much out of date very quickly, particularly in this ebullient area of atomic absorption spectroscopy. Other books in the series are proposed for thermoanalysis, nuclear magnetic resonance, X-ray fluorescence, gas-liquid chromatography, mass spectrometry, and so on. If this is a foretaste of the others in the series, I can but reply to the terminal two-word sentence of the text "Good luck" by saying "Thanks a lot".

T. S. West

Mathematics in Schools

The School Mathematics Project: The First Ten Years—Being Primarily the Collection of the Directors' Reports for the Years 1961–71. By Bryan Thwaites. Pp. x+266. (London: Cambridge University Press, 1972.) £3 cloth, £1.50 paper.

The SMP is a splendidly English institution: self-confident, pragmatic, free-enterprise. It started not in a Ministry of Education nor in a faculty lounge but in a Winchester garden. Its initial objective was "the evolution of a syllabus for the whole grammar school range of 11+ to 18, which will adequately reflect the modern trends and usages of mathematics; and the production of a complete set of associated textbooks and teachers' guides". Eleven years and nine directors' reports later, it has produced the books, run an impressive number of courses for teachers, fought and won against universities and examination boards, and expanded to include a wider spectrum of children.

The growth story is a fascinating one, told here in the reports by the project's rumbustious director, Bryan Thwaites. A short article at the end by deputy director Douglas Quadling gives interesting arguments for the inclusion of various topics—linear programming, networks, statistics, matrices, and so on. A great strength of SMP has been its flexibility: the period of self-torture in attempting to do all geometry by transformations is mercifully over, and there is a growing realization that some of the old techniques are still useful after all.

It is easier to criticize than to create. It could be argued that the children should have more relative consideration than the mathematics—how do SMP (and CSM and MME and SMG . . .) judge the degrees of difficulty and appropriateness of their selected topics? How, in fact, do children learn? But certainly the quickest way to a first answer to these questions is to write and see. Another criticism is that SMP has ignored the demands of other subjects, notably physics, but there is an element of "pot and kettle" here, and anyway there was so much to be reformed within a subject without looking sideways. A third criticism could be made of "export SMP"—what is the likelihood of this English venture being really appropriate elsewhere?—but mercifully this seems to be either on the decline or being handed over to the natives for treatment.

SMP will occasionally get its fingers burned (the story of the international project for computing in schools is hilarious, the countries concerned being England and an uncooperative Scotland) but it has played a tremendous role in getting English school mathematics into this century, and trial and error by dedicated teachers will probably continue to pay off for at least another ten years.

Geoffrey Matthews

Rational Enquiry

The Pluralist and Possibilist Aspect of Scientific Enterprise. By Arne Naess. Pp. 147. (Universitetforlaget: Oslo; George Allen and Unwin: London, July 1972.) £4.

Professor Naess can be pleased that the philosophical world is catching up with him. As he reminds us, the Vienna Circle of the 1920s and 30s was a somewhat missionary movement for "rationality" against reactionary forms of metaphysics, and it simply took physics as the paradigm of true knowledge. By contrast, Naess even then appreciated the plurality of genuinely scientific disciplines, and also of theories and approaches within a discipline, as of psychology.

Now, a long time later, he sees himself vindicated by the new pluralistic philosophies of science, notably of Kuhn, but with the implicit agreement of Lakatos. In this vein, he develops some slightly formalized descriptions of scientific choice and change, and also discourses widely over problems in the study of science.

His discussion is most coherent with English-language philosophy of science when it touches on Kuhn and the inescapable relativism of his conception of "scientific revolution" as a clash between incommensurable paradigms. Applying such a scheme to the writing of history and philosophy of science, including Kuhn, he shows that the inevitable paradoxes of self-reference are encountered. But handling these in the light of traditions of methodology of scholarship in general, he arrives at some genuinely interesting conclusions. Among these is that a truly comprehensive and consistent "point of view" cannot be explicitly chosen by an individual (for the conscious choice itself involves criteria belonging to one point of view or another). Hence the real changes that individuals experience in their world-views must occur from a more diffuse set of stimuli, and must proceed through less consistent intermediate stages.

A practical corollary of this conclusion is that pluralism, rather than exclusive domination by one or another system, is the only sane and effective style for science and rational enquiry in general. It is to be hoped that this message can be imparted to Professor Naess's new colleagues in the environmental field (where he now devotes his energies); simplistic philosophies of science are a luxury they cannot afford.

J. R. Ravetz

Complex Michelin

Chemical Industry: Social and Economic Aspects. By F. R. Bradbury and B. G. Dutton. Pp. ix+236. (Butterworth: London, October 1972.) £2.90.

EXPERTS assure us that in the not too far distant future the chemical industry will be Britain's single largest generator of wealth. Already it is among the leaders and its products have wrought profound changes in the general style of life. The industry has also had its share of criticisms of varied validity. In this interesting, no-nonsense, although somewhat misleadingly entitled book, two insiders explore the realities of successfully operating a major industrial enterprise.

The greatest public noise in recent years had been generated by those whose suddenly sensitized consciences discovered the environmental harm any industrial activity is liable to do. It is a welcome corrective to discover reality behind the slogans; that industrial activity is a matter of choosing the correct shade of grey rather than a re-run of *Paradise Lost.* Industry contributes to national wealth and thus to a high level of creature comforts the developed world has grown accustomed to, but it does so within the ideas, constraints and conditions imposed by society.

Perhaps it is a matter for emotional regret, but the work of industry does not ultimately depend on the inspired inventor leaping out of his bath, but rather on the patient cumulative efforts of solid, conscientious citizens. Thus Bradbury and Dutton, ex-ICI and ICI respectively, are particularly interesting on the multifarious skills needed all the way from production to final use; the roles of marketing and selling strategy, the tortuous route which takes a burgeoning idea to a multi-million pound factory complex, the use of complex analysis to achieve the correct compromise.

The social effects of the chemical industry are complicated and wide ranging and the current debate has progressed beyond considering the undoubted excellence of synthetic fibres and the existence of pharmaceutical products. It would have been illuminating if the book could have mirrored the concern of industry with secondary effects on society, both good and ill, and the change of values mediated through industry.

The book has been written principally for school leavers and their teachers. They will find an excellent Michelin guide to the complexities of modern industry, but rather less of the human excitement and concern which ought to be emphasized if industry is to obtain its share of the best in the age group.

There is a chapter on the individual in industry, but it is rather like a syllabus, a skeleton instead of the living animal. Yet there are plenty of facets to excite the humanistically inclined school leaver; for example, the generally excellent labour relations in the chemical industry and the sophisticated ideas now put in practice to make repetitious jobs more interesting and satisfying. Where are the great human battles that signalled nearly every major development, that gallery of larger than life figures that the chemical industry can boast of, men who may not have known anything about discounted cash flows but pitted their vision against existing society? And, indeed, where are the spectacularly bad decisions that are occasionally made *pace* computers, decision trees and risk analysis? In the last resort, industry and the effects of industry encompass but go far beyond machinery and techniques. They make statements about men in society, about hopes and realities, ambitions and prices paid for them. P. J. FARAGO

Pesticides as Pests

Environmental Toxicology of Pesticides. Edited by Fumio Matsumura, G. Mallory Boush and Tomomasa Misato. Pp. xiv+637. (Academic: New York and London, August 1972.) $17.50.

THIS book contains the published version of twenty-nine papers read at a United States–Japan seminar held in Oiso, Japan, in October 1971. This is not evident from the title, yet of the forty-eight contributors to this book, twenty-nine work in Japan, seventeen in the USA, one in Canada and one in Britain. Accordingly, what is being offered by Academic Press as a comprehensive work has cut out potentially valuable review articles from scientists outside the USA and Japan. One can imagine how much better this work could have been if, after using the conference as a basis, additional contributions had been obtained to fill the gaps in coverage.

Within these reservations, however, the book contains valuable contributions. The first three chapters deal with the impact of pesticides in Japan, United States and Britain, and these well prepared contributions vividly illustrate both the differences in uses of pesticides in these countries and their respective governments' action in monitoring and limiting the use of certain chemicals.

Further chapters consider mercury in the environment, chlorinated hydrocarbons, fungicides, organophosphates and carbamates. Other sections deal with light and microbial degradation of pesticides and the toxic effects of pesticides on wildlife. The final section, which is far too brief, skims over the considerations and feasibility of designing new pesticides. In this last section, very little information is given on insect sex pheromones and the reader is left with the incorrect impression that these substances are only known from Lepidoptera.

I have two general criticisms of the book. First, a work like this needs a well constructed index. Unfortunately this is not supplied. The index lists three references to methylmercury and only one for DDT, while BHC, dieldrin, endrin, aldrin and DDE do not even appear. Second, if this book is meant to include a review of the present situation, then I am afraid a number of persons have a poor knowledge of the literature. I hope and believe that scientists in Europe working in this field have a greater knowledge of international published work.

In general, this is a useful contribution, but it could have been so much better. J. C. COULSON

More Spectroscopy

Journal of Electron Spectroscopy. Edited by C. R. Brundle and T. A. Carlson. Volume I. Number I. Pp. 112. (Elsevier: Amsterdam, October 1972.)

DURING the last decade electron spectroscopy has become one of the most important techniques for the investigation of the electronic structure of matter. It has given information on the inner orbitals of molecules and the band structure of solids which has hitherto been unobtainable by conventional "photon" spectroscopy. The literature in the field has expanded to the point which has justified the initiation of this new bimonthly devoted to the subject.

The main fields it embraces are X-ray and ultraviolet photoelectron spectroscopy, electron energy loss spectroscopy, Auger spectroscopy and Penning ionization spectroscopy. Papers covering instrumental aspects, analytical applications, theoretical calculations of electronic structure, photoionization studies by mass spectrometry or ultraviolet absorption as well as relevant work on X-ray absorption and fluorescence are also acceptable for publication.

The first two numbers of this bimonthly journal have already appeared. They contain valuable articles by established workers in various branches of electron spectroscopy. If the quality is maintained in future issues there is no doubt that the journal will provide a unifying medium for many closely related techniques in electron spectroscopy.

W. C. PRICE

Soviet Environment

Conservation in the Soviet Union. By Philip R. Pryde. Pp. xv+301. (Cambridge University: London, November 1972.) £5; $12.50.

Environmental problems are becoming increasingly world wide and in need of a global approach. Little progress can be made to their solution, however, until each particular country has learned to manage its own ecosystem. The many different realms within "Spaceship Earth" differ markedly one from another, not only in physical characteristics and economic structures but, more importantly perhaps, in political ideologies, cultural traditions and in aspirations.

The Soviet Union is one such realm. With more than one-sixth of the Earth's land surface it is deeply concerned with the many problems related to the judicious management of its bountiful, but by no means inexhaustible, biotic and mineral resources. There are instances where damming, diverting, polluting, channelling, draining and other alterations in the aquatic environment have resulted in very adverse effects on important fishing resources. Forest felling has encouraged soil erosion, eliminated wild life habitats, increased stream sediment, damaged fish runs and altered local microclimatic conditions. Surface mining activities have destroyed forests and agricultural lands, induced soil erosion and often seriously polluted nearby streams. Ploughing or grazing on steep slopes, neglect of incipient gullies, improper cropping practices, downslope ploughing, and other poor agricultural practices have contributed to the erosion which now affects two-thirds of the cultivated lands of the USSR.

This study has, as its theme, the contemporary Soviet concern for the conservation of the natural endowments of the country in the face of past and present maltreatment of the environment. Early chapters discuss the historical background of natural resource management in Tsarist Russia and the Soviet Union. The administrative organization governing the use of each broad category of natural resource in the USSR is summarized and some of the major problem areas that have arisen out of the particular Soviet approach are selected for discussion.

Successive chapters deal with land and soil resources, nature reserves, wildlife and fish management, mineral and forestry resources and environmental pollution. The final chapter attempts an evaluation of the contemporary Soviet perception of what constitutes proper natural resource conservation and examines the political and philosophical implications of conservation practice.

One hundred and fifteen of the 300 pages are taken up with an extremely valuable bibliography of Soviet and foreign literature and a large and varied group of appendices covering key terminology, legal documents and resources and environmental data.

Inasmuch as the book represents one of the first broadly inclusive qualitative studies of Soviet conservation practices to be developed outside the USSR, it is to be warmly welcomed. It is unfortunate, though perhaps inevitable, that it should be so expensive.

G. Melvyn Howe

Exploiting Enzymes

Enzyme Engineering. Edited by L. B. Wingard, Jr. Pp. xiii+415. (Wiley: New York and London, October 1972.) £5.20.

The thirty reviews, by sixty-one contributors, are based upon two 1971 symposia in the USA. In section 1 the editor defines enzyme engineering as "the sum total of production, isolation, purification, immobilization, and uses of enzymes in a variety of reactor geometries". This section also includes valuable "Recommendations for Standardization of Nomenclature in Enzyme Technology".

The methodology of enzyme overproduction by microorganisms, discussed in section 2, is exemplified by the tonnage of proteases isolated. Cellulase utilization should now be seriously examined at large-scale pilot plant level. Dunnill and Lilly, in section 3, illustrate the future with a description of continuous techniques for disruption and recovery by, for example, multistream continuous chromatography, of several enzymes simultaneously. As one alternative to a mechanical technique they disrupt bacteria using lysozyme immobilized on soluble dextran (molecular weight 2×10^6), followed by ultrafiltration. No doubt other uses of soluble immobilized enzymes will follow. For enzyme separations, Porath mentions a new range of amphoteric ion exchangers and evaluates affinity chromatography.

The section on enzyme immobilization omits recent simplified techniques. Attainment of stability may require chemical modification of enzyme prior to immobilization, although Zaborsky disappoints us by providing no details of his own work to which he alludes. Section 5 covers kinetics and performance of enzyme reactors. Apparently, 500 columns, each of 1 ft^3 volume of immobilized glucamylase, would replace the total present enzyme production of glucose syrups from corn starch in the USA; but the economics of the process are questionable. On the other hand, Ford *et al.* describe a 10-ml. capacity recirculation reactor useful for immobilized enzyme kinetics studies.

The book also includes analytical techniques using enzyme electrodes and the potential for microencapsulated enzymes in therapy, and is an invaluable collection of data and ideas in spite of the regrettable absence of widespread commercial utilization of immobilized enzymes to date. The one such application, racemase in Japan, is, however, quoted repeatedly. Where is the profitable return for so much "biochemical ecstasy"? No one is prepared to divulge this yet. Is reactor operation in fact proving too expensive for some? In addition, natural enzymes, or multienzyme systems, may be superseded by synthetic ones sooner than many think (the "time bomb hanging over enzyme engineering"). Nevertheless, the future will be exciting if industry can be induced to make it so. The next symposium in summer 1973 should be fascinating!

This book is good value for money, but its author index is irrelevant and the subject index is almost useless due to its extreme brevity.

B. J. Gould
A. Wiseman

Shaping of Plants

Patterns in Plant Development. By Taylor A. Steeves and Ian M. Sussex. Pp. xvii+302. (Prentice Hall: Englewood Cliffs, New Jersey, October 1972.) $10.95.

The dust cover announces that this book presents a factual account of the phenomena of development in the vascular plants. The book is not, however, a dry documentation of anatomical events from zygote to adult. Instead it outlines the variations in structure that are encountered from Bryophytes to Angiosperms and presents experimental evidence for how environmental and endogenous chemical and physiological factors are believed to modify the pattern of development. Each of the seventeen chapters surveys a particular aspect of development, setting out the problems for the reader and pointing to areas of understanding which can profitably be expanded by future work. Each chapter concludes with a section of general comment and up to thirty-two selected references.

The essential plasticity of leaf form and regulation of shoot growth in relation to hormones from leaves and stem are nicely presented. The conversion of vegetative to reproductive apices is related to the change from indeterminate to determinate growth and is linked to biochemical activities of the meristem itself. The similarities and differences between root and shoot meristems are skilfully outlined as are considerations of differentiation of the plant as a whole. The origin and development of vascular elements, the special types of cells of which they are composed, and the role of hormones and sugars in their initiation are given considerable space. Two important chapters cover the formation and function of the cambium and the final chapter deals with totipotency and regeneration.

Throughout the book the question, "How do all these cell types differentiate in a coordinated way to produce the integrated, functionally efficient organism?" is presented and expanded in a particularly lucid and interesting way. The experiments described are well chosen to illustrate questions in plant development rather than to provide answers that are yet in doubt. The chapters on embryogenesis, the shoot apex and the origin of leaf and bud primordia are excellent examples of this approach. Now that there is already so much for the scientist to read, these authors must be congratulated on providing a valuable book that cannot fail to stimulate thought in students and research workers and arouse the interest of all those who work with plants.

DAPHNE J. OSBORNE

Quantum Mechanics

Quantum Mechanics: Principles and Formalism. By R. McWeeny. (*The International Encyclopaedia of Physical Chemistry and Chemical Physics. Topic 2. Classical and Quantum Mechanics Vol I.*) Pp. xi+155. (Pergamon: Oxford and New York, 1972.) £3.50.

ANOTHER "Introduction to Quantum Mechanics"? One's worst fears are aroused, for surely there are already quite enough of these. But Professor McWeeny's book justifies itself, and one's preliminary fears are not realized. First, as the author says, this is not an introduction, for the basic ideas of the quantum theory are assumed: it represents a revision course, with the opportunities that any revision course provides to give a more consistent account than is possible when the material is first being introduced to the student. Second, although its scope is limited (no one should try to say everything in 150 pages), it is definitely oriented towards the budding theoretical chemist rather than the theoretical physicist or applied mathematician; and to that extent it is not in competition with many other accounts of quantum theory.

Professor McWeeny writes as a master of his subject, with considerable form and control. He also writes well, so that this book is a pleasure to read. Its compass is limited, and we are told that it is to be the first of a sequence of four volumes dealing with the principles and techniques of quantum mechanics. With such a writer it would surely have been far better to let him write one large volume. The result would have been cheaper (this whole encyclopaedia is far too expensive for the very people it best serves): and he should not have had to stop short after an admirable account of transformation theory, momentum representation, single-particle spin, and the properties of linear operators in Hilbert space, waiting for successive volumes to deal with perturbation theory, group theory, many-body theory and scattering theory. Within the "brief" that he was given Professor McWeeny has done a splendid job: but the brief was not big enough.

C. A. COULSON

Metal Pi-Complexes

Metal Pi-Complexes. By Max Herberhold. Volume 2. *Complexes with Mono-Olefinic Ligands.* Part 1. *General Survey.* Pp. xv+643. (Elsevier: Amsterdam, London and New York, 1972.) Dfl. 250; $78.25.

THE author of this volume comes from a laboratory famous for its work on metal π-complexes—the Technische Universität, Munich. This present volume, Part 1, deals with the history of the subject and the earlier views on bonding; general methods of preparation follow. The main body of the text is devoted to a detailed systematic survey of mono-olefinic complexes. The main emphasis is placed on preparative aspects, but physico-chemical properties are quoted wherever necessary for an understanding of the structure. The olefins have been subdivided into hydrocarbons, for example, ethylene, and those possessing functional groups, for example, acrylonitrile. Spectroscopic and diffraction data, stability constants, current views on metal olefine bonding and uses in homogeneous catalysis, are promised for the second part.

The present volume includes the literature up to the end of 1968 (an appendix gives abstracts of 210 important papers which appeared during 1969 and 1970). I sympathize with the difficulties experienced in the writing and production of such a volume, but potential purchasers ought to know that the systematic literature survey ended about three and a half years ago.

About 1,900 references (which refer to both volumes), together with author and subject indices, are provided. The book is well written and translated. It contains a wealth of material, much of it in tabular form, and should provide a most useful reference work for the research worker. The very fact that the book is so detailed makes it relatively unsuitable as a teaching monograph for students. My main complaint is at the price: volumes of similar size are currently published at a price half or less of the present book. Otherwise, it can be recommended to workers in the field.

R. A. SHAW

Phosphorus Chemistry

Phosphorus - Nitrogen Compounds: Cyclic, Linear and High Polymeric Systems. By H. R. Allcock. Pp. xiv+498. (Academic: New York and London, May 1972.) $24.50.

THIS book has been written by a research worker who has made notable contributions to the subject, particularly in the field of high polymers. It is exceedingly well written; the style is clear and concise, and the account of the subject is balanced and critical; it is remarkably free from mistakes.

The volume deals with monomeric, cyclic oligomeric, and polymeric phosphazenes, as well as with phosphazanes. The author develops the thesis (shared by several crystallographers active in the field) that the conformations these molecules adopt are dominated by steric factors rather than by π-bonding, that is, that the bonding adjusts itself to the stereochemistry rather than the reverse.

One point which the author touches upon briefly and which undoubtedly will attain greater significance in the future is the differentiation between those properties of the molecules measured in the ground state, for example, by X-ray crystallographic, nuclear quadrupole and nuclear magnetic resonance studies, and those where the distribution of electrons, and possibly also the shape of the molecule, has been changed either by electronic excitation or complex formation, for example, in basicity studies.

The appearance of the volume is extremely opportune as phosphazenes seem to have broken through the inertial barrier and are beginning to fulfil their long foreseen industrial uses. They are now being manufactured on a considerable scale and have achieved *inter alia* uses in flameproofing.

The book can be highly recommended to the teacher as well as the research worker—academic and industrial. It can be recommended for student reading, although it is somewhat long for an undergraduate course. In view of the rapidly rocketing cost of books, the price is not excessive.

R. A. SHAW

NATURE Volume 241
FEBRUARY 2 1973

Mr Nixon's Non-Cultural Revolution

By all accounts, and from the appearances of recent weeks, President Nixon's visit to Peking last year has had a profound effect on his management of the United States Administration. Mao Tse Tung's cultural revolution seems in retrospect to have been founded on the belief that nation states should, from time to time, abolish the bureaucracy with which they are endowed and let another regroup in what may appear to be a more natural way. There is an element of this draconian policy in the way in which President Nixon has, for all practical purposes, abolished the machinery for the administration of science and technology in Washington. The Office of Science and Technology is to disappear, and its functions will be shared by the head of the National Science Foundation and by officials of the Office of Management and Budget. But at the same time, the President has gone a long way to dismantle the apparatus by means of which traineeships and fellowships have been provided by the federal government not merely for the encouragement of higher education and scientific research but for their sustenance. But however much the president may have been impressed with what has recently been happening in China, the analogy between China and the United States is not especially apt. The most conspicuous difference between Mao Tse Tung's sweeping away of the old bureaucracy and Mr Nixon's efforts in the past few days is that the former was a radical assault on the establishment but that the latter is a carefully controlled dismantling of what exists. Under Mr Nixon's proposals, there will be few opportunities for the forces which can contribute to the continuing evolution of American society to regroup themselves in advantageous ways—they will have to live within the confines of an extremely straitened budget and within an administrative framework which the White House appears determined to control. Given that much of what the present president has been doing and has announced in his new budget (see page 303) is hostile to intellectual causes, it is fair to say that he has launched not a cultural revolution but the opposite.

What matters about the dismantling of the Office of Science and Technology is not the decision itself but the way it has been done and the motives which have so far been inadequately disclosed. For basic science, the overriding question is which part of the federal government's machinery will be empowered to urge that there should be a continuing federal commitment for basic research, especially at the universities. In the 1950s, Dr James Killian, Science Adviser to Presidents Truman and Eisenhower, persuaded the federal government that it alone could shoulder the obligation to see that basic science flourished and, with the help of people such as Dr Vannever Bush and agencies such as the Office of Naval Research, the National Science Foundation came into being. With the election of President Kennedy and the appointment of Dr Jerome Wiesner as Science Adviser, the Office of Science and Technology became an institution in its own right, concerned with technical studies of all kinds but in particular with presenting the case for basic science at a more influential level in the bureaucracy than the National Science Foundation (in the last resort an appendage of the Department of Health, Education and Welfare) could manage. As things have turned out, there is a case for thinking that the Office of Science and Technology is indeed unnecessary operating agencies ought, in a good Administration, to be free to argue their own cases and should in any case be sufficiently well provided with technical people to understand the technical implications of what they do. The trouble is that the abolition of the Office of Science and Technology is not now accompanied by a declaration from the federal government that the interests of basic science will be safeguarded by the National Science Foundation, nor by an affirmation from the White House that graduate education must be a federal responsibility, but instead by a continuing ambiguous exhortation to the National Science Foundation that its work must be in some sense relevant.

The assault in the new budget on the federal government's provision of traineeships and fellowships will be especially harmful. For the best part of a decade, the National Institutes of Health have by these means powerfully encouraged the development of university research in all branches of medical science but especially in cancer research, to which the Administration still attaches great importance and on which it plans to spend substantial funds. The truth is, however, that it would not be feasible now for the President to say in his budget that the attack on cancer will be prosecuted vigorously in the years ahead if it had not been for the way in which the NIH have spent money on traineeships and fellowships in the past decade. Here, if only the Administration had had the wit to understand, would have been a splendid object lesson in the value of basic research. And although, with the passage of time, it may be possible for universities to find other means of supporting graduate students, there is no doubt that in the immediate future the attenuation of the programmes of the NIH and the NSF in graduate education will harm not merely the potential students but the universities at which they might have followed graduate courses.

How should basic science in the United States respond to the changes now in prospect? One tendency that the universities must be prepared to meet has close parallels with what has recently been happening in Britain. The pressure on funds for research is already so great that universities are being forced somehow to discover a more rational pattern for the sharing of their work. Luckily, there are ways in which, in principle at least, this may be done without undermining the fabric of the university system—the University Grants Committee and the Science Research Council between them have the instruments of selectivity and concentration in their hands. It will be best for everybody if American universities somehow devise for themselves machinery for regulating their development at a time of contraction, not growth.

Along with this it is important that the academic community should seize every opportunity to ask searching questions about the federal government's now truncated policies for research and development. Is it sensible that the National Science Foundation should be so wedded to applied research when it has yet to demonstrate that it can function as an entrepreneur of innovation more effectively than the other operating agencies of the federal government? Is it proper that so much of the spending of the National Aeronautics and Space Administration should be committed to space flights when what is spent on basic science is being reduced? In the months ahead, it is essential that academics should come out from the covers and urge these and other arguments on the federal government. If in the process they find it necessary to take Senator Edward Kennedy to task for the inconsistencies in his Science and Technology Bill, no harm will have been done.

Another Pretty Flame

A HIGH-RANKING newsman from the BBC confessed on late night television last year that the BBC's television news had lost its head over the eruption of Mount Etna. Too much time, he felt, had been devoted to films of fiery lava, not because it ranked high in social, economic or political importance, but because it was so photogenic.

Now that the Helgafell Volcano in the Westman Islands off the coast of Iceland is claiming chunks of the six, nine and ten o'clock news shows, what is really at fault with television's coverage of such events is plain for all who care about science to see. There is no attempt at all to explain why Iceland should be visited by this form of natural catastrophe so often. When there is a pseudo-science story, such as a man walking on the moon, the television makers trot out their science correspondents, import geologists and physicists and have a field day making papier mache models and diagrams. But none of this treatment is, in fact, given to a genuine scientific news event. No one would know, watching the shooting fires and floating pumice on colour television, that new understanding of the forces at work on the mid-Atlantic ridge and other plates of the earth's crust has been one of the major scientific advances in recent years.

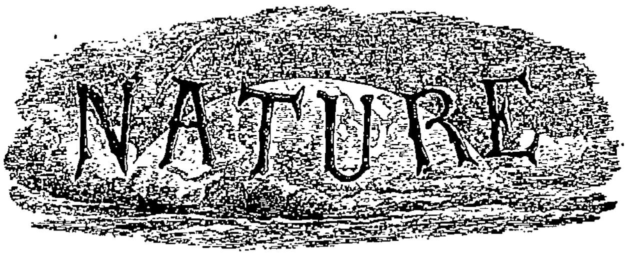
Television is feeding the public the primitive idea that nature is random and capricious. It is doing this particularly in children's programmes. The BBC's vaunted after-school programme. "Blue Peter", has been conspicuously lazy in its approach to science. It devoted a whole segment of a show recently to the Icelandic eruption with no mention of the mid-Atlantic ridge. To fill out its time, the programme dug out old film to show that the Blue Peter team had looked lava in the face at Mount Etna too. The same programme, some days earlier, had discussed tropical fish from the point of view of their ability to harm man. Some fish stung, some bit and others (sharks) could chew people all to bits. The fact that these natural defences were of some advantage to the fish was not discussed.

There has been a voguish anti-rationalism in many television documentaries ostensibly devoted to science and technology which is worrying. For example, the recent programme on the common fear of travel by air seemed to give legitimacy to the fear, on the grounds that many people suffer from it. (Its title was "The Only Way to Go".)

Professor Velikovsky also came in for some less-than-objective treatment from television recently. There was Velikovsky and his theories, on the one hand, and conventional astronomers and their theories on the other, and glowing sunsets suggesting worlds in collision to bind the two together. The science programme, "Horizon", has followed a doomsday line lately.

It is being said that Dr Bronowski's new series, "The Ascent of Man", will correct the anti-science swing inside the BBC. That would be good, but there still needs to be some new thinking on science news itself. There are reasons why the earth's crust bursts open where it does and why earthquakes occur in some places and not others. News editors who just show the pictures without explanation are doing as much disservice to the public as if they showed photographs of bombs and victims without mentioning that there was a war going on.

100 Years Ago



SEDGWICK

GEOLOGY has lost her veteran leader! While yet firm in intellect, full of kind and generous feeling, and occupied on the last pages of the latest record of his labours, in the ninth decad of a noble life, Sedgwick has gone to his rest. Under the shadow of this great loss we look back through more than half a century, and behold no more conspicuous figure in the front ranks of advancing geology than the strenuous master workman, the eloquent teacher, the chivalrous advocate of science, who has now finished his task. Severe illness, borne with fortitude, had gradually withdrawn him from scenes once brightened by his ever-welcome presence, but could not tame the high spirit, or cloud the genial sympathies which had won for him, more than for other men, the loving admiration of his fellows in age and followers in study. Rarely has a patriarchal life been crowned with such enduring and affectionate respect.

From Nature, 7, 257, *February* 6, 1873.

OLD WORLD

Makings of a French Science Policy

FUTURE French science policy is outlined in the pages of *La Recherche* this week where the leaders of the chief political parties outline their views on science in France in preparation for the general election in March. If election promises are kept, the outlook for science is none too bright.

M. Jean Charbonnel, minister for industrial and scientific development, seems fairly happy with the *status quo*. The organization of French science is more than adequate he says, and the existing problems are simply administrative ones. Medium and small companies must be encouraged to undertake research, even though the 1973 budget has produced a cut in the sixth five-year plan (see *Nature*, **240**, 64; 1972). By the end of the plan (1977) he hopes that the growth rate in science will be back on course, and he points out eagerly that the *grands programmes* of space, computing and nuclear power have been kept viable in spite of budget cuts.

Discussing European problems, M. Charbonnel reaffirms France's desire to see a European space policy, pointing out that if the proposal for the L3S launcher (put to the European Space Conference on December 20) goes through, the project will be centred around French industry and technology, demonstrating the quality of French skills.

Nonetheless M. Charbonnel singles out research on the quality of life as the most important area for study.

The views of the left-wing alliance—a union of the communist and socialist parties—are represented only by the opinions of Roland Leroy, secretary of the central committee of the French Communist Party, as M. Francois Mitterand, the national secretary of the Socialist Party withdrew his replies to *La Recherche*'s questions at the last moment. This withdrawal will only feed the fears of those who believe that French politicians are largely uninterested in science policy, and the fact that the leftist alliance may well gain seats in the forthcoming election presents, to many scientists in France, a worrying prospect if Mitterand's actions reflect his interest.

Leroy maintains that, given power, he would completely reverse French science policy, at the same time increasing expenditure on science to 3 per cent of the gross national product. Numbers of French scientists should be increased and most should work in the public research organizations, while greater efforts should be made for European cooperation. Leroy would also put an end to work on France's atomic bomb, directing the work of the Commissariat à l'Énergie Atomique, which he would expand, to more peaceful ends. Leroy, too, would encourage work designed to improve social, working and living conditions.

Michel Poniatowski, secretary general of the Federation of Independent Republicans, and as such a member of the majority, agrees that politicians tend not to be interested in science and blames this on the failure of scientists and civil servants to involve the public in science. He is heavily critical of the way the science plan is developed over a five-month period each year without any knowledge of the final budget within which it will have to operate.

Poniatowski also argues that fundamental science is already well financed, but urges that applied science should receive more attention, particularly in the universities.

The French space programme receives some caustic criticism, M. Poniatowski warning that France must not go ahead alone with a policy that is beyond the limits of its resources. On the other hand oceanography should receive more attention. Poniatowski would also work to see research scientists and their views included in government deliberations.

Michel Rocard, national secretary of the United Socialist Party, argues that since M. Pompidou came to power there has been no research policy, and he is highly critical of the way American nuclear power companies have been allowed to overtake French expertise. The money poured into the CEA for twenty-five years, he says, has been to no purpose.

The liveliest selection of views offered by the political leaders are those of Jean-Jacques Servan-Schreiber, although his chances of putting them into effect are slim. Science for him is a sacred cow. There is a "plethora of research scientists", he complains; the numbers working for CNRS should be cut, their expertise being distributed among the universities, technical colleges and industry. Only the best qualified research scientists should work in public organizations, and as much as one-fifth of the science budget should be poured into private industry. Much more research should be run on the American contract basis, he says, and the bureaucracy involved in running science at present should be heavily cut down.

SELECT COMMITTEE

Reactor Safety Queried

THE Select Committee on Science and Technology is becoming increasingly concerned about the safety of nuclear reactors, particularly in the light of rumours that the government is to buy light water reactors from the USA.

The committee's concern is underlined by the decision to have a special showing in the next few days of last week's *World in Action* programme on the United States nuclear industry which brought allegations that the light water reactors are not as safe as they might be to the fore again.

This week, however, the committee was assured of the safety of the British steam generating heavy water reactor (SGHWR) by Mr S. A. Ghalib, managing director of The Nuclear Power Group (TNGP), when the group gave evidence to the committee. The select committee has long favoured the SGHWR and is eager to see it built for the Central Electricity Generating Board, and TNPG made it clear that it is equally enthusiastic. Mr Ghalib said that there is no doubt that the SGHWR is safer than either the pressurised water reactors or the boiling water reactors. Operating experience of the 1 MW prototype at Winfrith and the fact that SGHWR is built on already proven technologies combine, he said, to make development risks minimal.

The group welcomed the proposed merger of the two existing consortia, urging that the new company be made up of three components—themselves, British Nuclear Design and Construction and British Nuclear Fuels. The sooner the reorganization takes place the better according to Sir Edwin McAlpine, TNPG's chairman. Sir Edwin also made it clear that once the reorganization is complete, plans can begin for the formation of an all-European nuclear company, probably the result of an amalgamation of the new British company and Kraftwerk Union of Western Germany. This company, Sir Edward said, would, in time, probably be the only all-European company operating in Europe, although competition could be expected from Westinghouse and GEC subsidiaries.

POST APOLLO

ESRO joins in

THE ESRO council last week decided to authorise the establishment of a "special project" to develop a sortie laboratory that will fly with the NASA space shuttle in the 1980s.

The estimated cost of the sortie laboratory is between $250 million and $300 million and so far Germany, Italy, Belgium and Spain have agreed to participate. It is expected that other countries will signify their intentions to join now that the decision to participate has been taken.

ESRO is at present instituting a series of studies on the design of the sortie laboratory which are expected to be completed by the end of 1973. The organization intends to carry on the special project through the final design stage to the development stage and it is provisionally planned to deliver a flight unit to NASA in 1979.

The sortie laboratory will consist of two parts one of which will be a pressurized capsule that will accommodate up to six people and the other an unpresurized unit that will be suitable for conducting experiments for up to 30 days in space. The laboratory will be carried into orbit by a shuttle orbiter and will remain attached to the shuttle during its entire time in space. At the end of each mission the orbiter will land at the launch site and the laboratory will then be removed and prepared for the next mission.

As yet Britain has not decided whether to join her ESRO partners in this scheme. A spokesman for the Department of Trade and Industry said this week that the possibilities were being actively considered but that no decision should be expected in the near future.

ESRO's decision to join the post Apollo programme comes more than eighteen months after the original offer was made.

WATER RESOURCES

A Watered-down Bill

TEN regional water authorities and a National Water Council are to be set up under the government's Water Bill published last week (HMSO, £0.63).

The bill will bring a long overdue rationalization to the 29 river authorities, 160 water undertakings and 1,300 sewerage authorities that currently make up the water services in England and Wales.

There were few major changes in the bill's clauses from the proposals first circulated by the Department of the Environment in December 1971, but the local authorities, which had resented losing their control of sewerage functions and water supply to the new RWAs, are thrown a sop in that they will have a majority of the seats on each authority. As a result the consumers' councils that were part of the original proposals and were intended to represent the views of the local authorities and other interests, have been dropped.

The National Water Council remains all that the Water Resources Board and its allies have feared it would be. The council is to be purely advisory, without a strong staff of its own.

Pressure on parliamentary time has resulted in the British Waterways Board, which is responsible for canals in Britain, receiving a reprieve, but one which may well be withdrawn later. Legislation to tighten up pollution control has also been dropped for the same reason, although the government promises to make amends when it introduces its wide ranging environmental bill which will also cover noise, air and waste pollution.

As a gesture towards conservation the Natural Environment Research Council is to be made responsible for informing the regional water authorities of any sites of special interest within their jurisdiction which may not be nature reserves but which may be affected by the authorities' activities.

POLLUTION

Cleaner Air

ALTHOUGH Lancashire, Cheshire and the High Peak District of Derbyshire are among the most polluted areas in Britain, the average concentrations of smoke and sulphur dioxide in the atmosphere have decreased by 55 per cent and 40 per cent respectively during the past decade (*National Survey of Air Pollution, 1961–71*, HMSO, £3.50).

The average concentration of smoke and sulphur dioxide in the north-west during the 1968–69 and 1969–70 winters was 143 and 178 micrograms per cubic metre respectively, in urban areas. In the industrial part of South Wales, however, only three sites out of twenty-six had smoke levels greater than 50 micrograms per cubic metre and only two sites showed the sulphur dioxide level to be greater than 100 micrograms per cubic metre. But in the south-western part of Britain, Wiltshire, Gloucestershire, Dorset, Somerset, Devon, Cornwall and the Scilly Isles the comparable levels of smoke and sulphur dioxide were 13 and 39 micrograms per cubic metre respectively.

The surprisingly low figures for South Wales are due to the low volatile matter and low sulphur content of the coal mined in this area.

UNIVERSITIES

Better than Evens

A MARKED increase in the number of students applying for university places to read medicine and a drastic decline in the numbers of students wanting to read mathematics, physics, chemistry and some engineering subjects are reported in the tenth report of the Universities Central Council on Admissions published last week.

Table 1 Comparison of Number of Candidates Applying for University Places in 1971 and 1972

Subject	Number of applicants 1971	Number of applicants 1972	Number admitted* 1972
Medicine	8,971	11,177	2,955
Mathematics	6,041	5,451	3,687
Physics	3,017	2,807	2,280
Chemistry	3,405	2,857	2,466
Engineering and Technology (total)	17,644	16,859	9,035

*Admitted through UCCA only. Some Scottish universities do not participate fully in the UCCA scheme.

The increase in the prospective medical students from 8,971 in 1971 to 11,177 in 1972 is the more striking because the total number of British applicants for places in all departments fell from 114,968 to 113,966. But the total number of applicants increased slightly because the number of overseas candidates for places increased from 9,016 in 1971 to 10,393 last year. Of this total, the eighty-one institutions which participate in the UCCA scheme admitted 60,510 students.

Although there were almost two applicants for every university place last October 2,744 places were left unfilled. Of these vacancies, 1,400 were in engineering and technology, and more than 600 in the sciences, but there were also more than 840 vacancies left in the Arts. On the positive side, medicine, dentistry and health departments accepted 224 more students than they had planned to take, so that 5,397 students started courses in these subjects.

UCCA handled 21,585 students in its clearing scheme once A-level results were known, and the council managed to find places for more than 6,500 of these. But 8,682 students were not referred to a university either because their A-level grades were not good enough or for some other reasons.

Even though on the face of it it seems that there were almost two applicants for every university place, UCCA stresses that the situation is in fact better, for between 15 and 20 per cent of the applicants did not have the minimum examination qualifications required by any university and 13 per cent of the applicants were applying for the second or even third or fourth times.

NEW WORLD

Belt Tightening in Store for US Science

by our Washington Correspondent

ANOTHER period of financial starvation is in store for science and technology in the United States. That is the prospect held out by President Nixon's austere budget for the 1974 financial year (which starts on July 1 this year), which was sent to Congress earlier this week. The budget proposed an overall increase in expenditure on research and development which is clearly insufficient to keep pace with inflation and, moreover, it is also made clear that cutbacks in some areas—notably space and some biomedical research—will not wait until next year, but will be put into effect immediately.

The overall strategy for science and technology outlined in the budget is to allow increases in areas of research likely to benefit society—energy, transportation, cancer, disease of the heart, lungs and blood vessels, and drug abuse are all set for relatively large increases in research money. But this largesse will be offset by cutbacks elsewhere. And, in spite of the fact that the United States is at last moving towards a peacetime economy, defence-related research and development is again set for a large increase. Basic research comes off particularly badly in the budget.

The reason for such a gloomy outlook for science and technology is that after proposing expansionary budgets to Congress for the past two years, President Nixon has decided to slam the brakes on public expenditure in order to make good his promise not to increase taxation. In effect, he has partially abandoned the teachings of John Maynard Keynes and returned to the era of balanced budgets.

As a first step, he will slash more than $11,000 million from federal expenditures this fiscal year—which is already more than half way through—to keep total government spending below $250,000 million. And the budget which he has proposed for 1974 sets an upper limit of $268,700 million, which is an increase of about 7.5 per cent, most of which will be swallowed up by inflation and by commitments made in previous years. Sharp reductions are planned for many programmes, but social services, agricultural subsidies, unemployment assistance and President Johnson's great society programme figure prominently among the casualties. In relation to these programmes, science and technology fare relatively well.

The total budget for research and development is due to increase from $16,500 million last year, to $17,100 million this year, and to reach $17,430 million next year. Not all of this money will be spent immediately, however, since obligations often extend over several years, and the actual spending pattern presents a rather more alarming picture. Total expenditures on research and development last year came to $16,103 million, this year they will drop to $15,886 million, and pick up again next year to $16,790 million (see Table 1). The effects of this dislocation in spending will be most severely felt

White House Unveils the Plan

by our Washington Correspondent

PRESIDENT NIXON has finally announced his intention to dismantle the science policy apparatus that was set up in the White House by Presidents Eisenhower and Kennedy during the panic that followed the launching of Sputnik. As expected (see *Nature*, **241**, 234; 1973), the Office of Science and Technology is to be abolished and the National Science Foundation will become the focal point in the federal government for the formulation of US science policy.

The post of Science Adviser to the President, which was vacated by Dr Edward E. David earlier this year, will also be scrapped and Dr H. Guyford Stever, director of the National Science Foundation, will assume the role of chief science adviser to the White House. He will advise the President through Dr George Shultz, Secretary of the Treasury and the President's Assistant for Economic Affairs. The changes were formally announced in an executive reorganization plan which was sent to Congress at the end of last week.

Congress has 60 days in which to comment on the plan and if it is not blocked it will be put into effect on July 1 this year. Although the plan does not mention the President's Science Advisory Committee, it is understood that it will be abolished along with the Office of Science and Technology. Dr Stever, in theory, will be called upon to advise on policies involving all types of science and technology, but it is expected that advice on military research and development will usually come from the Department of Defense and the National Security Council will also take on some additional responsibilities in this area. Similarly, the director of the National Institutes of Health will probably continue to be the chief source of advice to the White House on biomedical research.

The reorganization plan also involves scrapping the National Aeronautics and Space Council—the White House Committee with the vice-president as chairman which has the task of coordinating policies for space and aeronautics. The NASC was originally formed in response to the launching of Sputnik, and its duties have largely been carried out by the National Aeronautics and Space Administration during the past few years.

Although the reorganization plan has at last been published, several questions still remain about the new structure. For one thing, Dr Stever will be faced with at least a potential conflict of interest in being director of a federal agency, and at the same time offering advice to the Office of Management and Budget about how the science budget should be divided. At the same time, the National Science Foundation will not be getting any new staff or an increase in budget to help it carry out its new functions. Dr Stever said last week that the Foundation's budget for 1974 will allow it to increase its staff by about 20 people, but the extra staff is needed for existing NSF programmes such as RANN (Research Applied to National Needs). If new staff members are taken on specifically for the new science policy functions, presumably it will be at the expense of other NSF activities.

Asked last week when he was first brought in on discussions of the plan, Dr Stever replied, "About two weeks ago". The plan was therefore drawn up in the White House and presented to the National Science Foundation more or less as a *fait accompli.*

Table 1 Conduct of Research and Development (in millions of dollars)

	Obligations			Expenditures		
	1972 actual	1973 estimate	1974 estimate	1972 actual	1973 estimate	1974 estimate
Defense—Military functions	8,294	8,338	8,808	8,117	7,873	8,333
National Aeronautics and Space Administration	3,183	3,383	2,995	3,373	3,008	3,066
Health, Education and Welfare	1,763	1,832	1,969	1,513	1,670	1,873
Atomic Energy Commission	1,298	1,359	1,411	1,298	1,359	1,411
National Science Foundation	456	461	516	418	423	446
Transportation	351	367	425	274	290	359
Agriculture	353	378	351	349	360	343
Interior	220	259	262	210	262	255
Commerce	184	214	211	165	179	187
Environmental Protection Agency	122	177	138	133	146	164
Veterans Administration	71	76	78	66	71	75
Housing and Urban Development	47	43	71	47	43	61
Justice	24	39	54	13	30	46
All other	134	184	141	127	173	171
Total, conduct of research and development	16,500	17,110	17,430	16,103	15,886	16,790
Total, conduct of research	6,483	6,689	6,737	6,169	6,300	6,555
Total, conduct of development	10,017	10,421	10,693	9,934	9,586	10,235

in the Department of Defense, NASA and NIH.

Obligations for science and technology will at least increase both this year and next, but at rates of 3.7 and 1.9 per cent respectively, they will obviously be insufficient to keep pace with inflation, which is running at between 4 and 5 per cent. Moreover, if those figures are contrasted with the promises made a year ago in the 1973 budget, a better idea of the extent of the freeze in science and technology can be gained. The 1973 budget proposed increases in obligations for research and development from $16,500 million in 1972 to $17,800 million this year. Similarly, expenditures were set to increase from $15,800 million to $16,480 million. The estimate for obligations this year is thus $700 million less than the estimate made a year ago, and the proposed budget authority for next year will be $400 million less than the total originally proposed for this year.

The $600 million difference between the original and the revised estimates for expenditures on science and technology in the 1973 fiscal year gives some indication of the effect on research and development of the $11,000 million cutback in total federal expenditure which President Nixon has ordered—more details of the cutbacks will be sent to Congress later this week. It represents a reduction in the science budget of nearly 4 per cent which, although it will result in some severe dislocations, is rather less than expected.

Expenditures on science and technology unfortunately fall in the category of relatively controllable federal outlays—only about $87 million could be cut from federal expenditure this year, the remainder of the budget being made up of commitments carried over from previous years, or of expenditures such as pensions and veterans' benefits which cannot be reduced. The $11,000 million total cut in federal expenditure thus amounts to about 13 per cent of the controllable funds, and the 4 per cent cut in the science budget is therefore relatively mild. At least one official of the Office of Science and Technology has suggested that the OST can be given some of the credit for preserving the science budget from the full weight of the axe. Whether the new arrangements announced last week (see box) would be equally effective is a moot point.

The outlook for academic science has also been soured by financial stringencies this year and the promise of belt tightening next year. Expenditures by the federal government in science departments of colleges and universities are expected to increase by 4.7 per cent this year, and by 4.9 per cent between this year and next (see table 2). Such increases are barely sufficient to keep pace with general inflation, and clearly too small to account for the so-called sophistication factor. Moreover, they are considerably below the estimates made a year ago—the 1973 budget estimated about a 10 per cent growth in expenditures on academic science between 1972 and 1973, with the 1973 figure climbing to $1,964 million.

Although total obligations for science and technology are set to increase by only $320 million between the present financial year and 1974, defence research alone is scheduled for an increase of $370 million. Moreover, research and development related to the production of energy is due to be increased by $130 million, research into cancer and heart disease is set for a $92 million increase, and research related to transportation, reducing loss of lives and property from natural disasters, and curbing crime and drug trafficking is scheduled for an increase of $115 million. Clearly, therefore, other fields are being cut back to accommodate the increases.

The following are among the more prominent casualties:

- Training grants and fellowships at the National Institutes of Health are being abolished and nearly every research institute apart from the politically sensitive National Cancer Institute and National Heart and Lung Institute will suffer an absolute cut in operating expenses next year. Moreover, the Administration is now proposing to slash nearly $87 million from its original budget request for the present fiscal year for all Institutes except for Cancer and Heart and Lung (see page 306).

- Budget cuts in the National Aeronautics and Space Administration, which were announced earlier this month (see *Nature*, **241**, 83; 1973), will result in the cancellation of the High Energy Astronomy Observatory programme, development of nuclear propulsion, and work on communications satellites. The space shuttle and some aeronautical research will also suffer small budget cuts (see page 306).

- Agricultural research is being reorganized, and cut drastically both this year and next. The total budget authority for the agricultural research service will decline from $228.5 in 1972 to $205.0 this year and $185.8 in 1974. The chief move will be to concentrate agricultural research in fewer facilities and to drop projects considered to be of low priority. The implications for universities and colleges are not yet clear.

- The Administration is continuing its policy of reducing direct support of graduate students by finally abolishing the National Science Foundation's

Table 2 Research and Development in Colleges and Universities (in millions of dollars)

	Obligations			Expenditures		
	1972 actual	1973 estimate	1974 estimate	1972 actual	1973 estimate	1974 estimate
Health, Education and Welfare	874	885	935	721	765	839
National Science Foundation	374	378	423	342	347	365
Defense—Military functions	212	219	218	219	225	219
National Aeronautics and Space Administration	119	117	114	131	123	119
Atomic Energy Commission	85	84	87	85	84	87
Agriculture	88	96	77	79	88	73
All other	116	128	143	94	118	134
Total	1,868	1,907	1,997	1,671	1,750	1,836

traineeship programme and decreasing its graduate fellowship programme. The foundation's basic research support programmes are, however, set for a modest increase.

- A death warrant has been written for yet another high energy accelerator —the Cambridge electron accelerator— and the operating budgets of every accelerator except the 200 BeV machine are being cut. The total operating budget for high energy physics is set to increase by $4.1 million between 1973 and 1974. But the National Accelerator Laboratory is scheduled for an increase of $9.8 million—it will be the first full year of operation of the 200 BeV machine—the Cambridge electron accelerator will only get $600,000 and will be phased out, and the budgets of the Alternating Gradient Synchrotron, the Zero Gradient Synchrotron, the Bevatron, the Stanford linear accelerator and general research and development will be reduced by the following amounts: AGS—$400,000, ZGS—$1.2 million, Bevatron —$1.8 million, SLAC—$750,000, and general research and development—$150,000.

President Nixon's budget now goes to Congress, where it has to go through the annual authorizations and appropriations ritual. Although there will be no shortage of battles over many of its provisions, it is unlikely that Congress will be either willing or able to influence the total amount proposed for science and technology, for two chief reasons. First, the expenditure cuts proposed for the present fiscal year result chiefly from the fact that the Office of Management and Budget has impounded funds already approved by Congress. Unless such action is judged unconstitutional—its constitutionality is being challenged in the courts in at least two specific cases (see *Nature*, **240**, 436; 1972)—Congress at present has no recourse. And second, President Nixon has served notice in no uncertain terms that he will stick to the expenditure limit of $268.7 million which he has proposed for next year. Congress thus seems to have two options: either it can devise some mechanism by which the appropriations committees can reorder the priorities in the budget, but stay below the ceiling prescribed by President Nixon, or it can increase appropriations as it sees fit, only to have them vetoed by Nixon or the extra funds impounded by the Office of Management and Budget.

Past experience suggests that Congress will probably take the second course, and continue to do battle with President Nixon over his power to impound funds—a variety of bills seeking to limit such power have already been introduced. But in either case, it is unlikely that the general trends in the portion of the budget allocated to science and technology will be altered. US science is thus clearly heading for yet another period of financial stringency.

NATIONAL SCIENCE FOUNDATION

Caught in the Squeeze

by our Washington Correspondent

THE budget for 1974 gives the National Science Foundation modest increases in its funds for the support of basic research and a larger helping for its applied research activities. But the overall increases proposed for the foundation are insufficient to keep pace with general inflation and clearly too small to take account of the so-called sophistication factor which drives up the cost of scientific research.

Nevertheless, the foundation has probably come out of the budgetary process with as much cash as can be expected in the light of the squeeze on all items in the federal budget. Its budget will increase from $597.7 million in 1972 to $610 million this year and to $636.5 million in 1974 (see Table 1). The Office of Management and Budget has impounded $62.4 million of the foundation's funds for the present fiscal year, as part of President Nixon's plan to hold overall federal expenditure down to $250,000 million, the chief cuts being made in the foundation's education and graduate student support programmes. That accounts for the fact that the foundation will have about 10 per cent less money available this year than Congress appropriated.

As far as basic research support is concerned, the budget asks for $275 million next year, up from $261 million this year and $248.6 million in 1972. Within this total, all branches of science are scheduled for modest increases and none has been cut back. Nevertheless, the total being requested for 1974 is exactly the same as the original request for 1973, and so in effect the increases requested a year ago are being spread out over two years.

The foundation's applied research activities fare a little better, however. Requests for the programme of Research Applied to National Needs (RANN) total $79.2 million in 1974, compared with estimated expenditures of $70.0 million this year and $53.8 million a year ago. The Experimental Technology Incentives Program is also set for an increase, from $15 million this year to $18 million next—this is a new programme launched this year in conjunction with the National Bureau of Standards. The NBS's share of the venture is due to be increased from $7 million in 1973 to $8 million in 1974.

The graduate support provided by the National Science Foundation is again scheduled for a decrease, from $14 million this year to $9.2 million next, a cut which reflects the fact that the NSF graduate traineeship programme is being abandoned at the end of 1973. As for education improvement, this is set for an increase of some $13 million, to $60 million next year. The chief reason for the exceptionally low figure for 1973 is that the Office of Management and Budget withheld $30.8 million of the funds appropriated by Congress for this purpose.

During the past few years, a ritual has been established in which the authorizations committees in Congress increase the foundation's budget for education and graduate support, and the Office of Management and Budget withholds the increases. Since the committees earmark the money for those specific programmes, none can be transferred to other NSF activities and the foundation winds up with less money than it would if the committees had left it alone. Whether the same farce will be repeated this year remains to be seen, but the foundation's budget clearly has no room at all for further cuts.

Table 1 NSF Budget (in thousands of dollars)

	1972 actual	1973 est.	1974 est.
1. Scientific research project support	248,574	261,001	275.000
2. National and special research programmes	85,886	114,740	99,600
3. National research centres	39,735	39,538	48,000
4 Computing activities	12,544	10,000	10,000
5. Science information activities	9,711	8,300	8.300
6. International cooperative scientific activities	4,245	4,700	6.200
7. Research applied to national needs	53,767	70,000	79.200
8. Intergovernmental science programme	1,078	1,000	1,000
9. Institutional improvement for science	20,961	9,000	9,000
10. Graduate student support	20,340	14.000	9.200
11. Science education improvement	73,388	47.000	60,000
12. Planning and policy studies	2,929	2.000	2,000
13. Programme development and management	24,562	28,722	29.000
Total direct programme	597,720	610.001	636.500

NIH

The Bubble Bursts

by our Washington Correspondent

THE crusades against cancer and diseases of the heart, lungs and blood vessels have finally taken their toll on other areas of biomedical research. The budget presented to Congress this week calls for large increases in the budgets of the National Cancer Institute and the National Heart and Lung Institute, but proposes sharp cutbacks in funding for all other institutes in the Institutes of Health. Moreover, the Administration has proposed that NIH training grants should be phased out and that federal support for the training of doctors should be sharply curtailed.

These proposals are likely to be fiercely resisted by Congress, which has consistently backed large increases in funding for biomedical research during the past few years, but there seems little prospect that Congress will be able to prevent at least those decreases which are due to be brought into effect immediately.

President Nixon's budget proposes that the budget of the National Cancer Institute should be increased to $500 million in 1974, and that of the National Heart and Lung Institute should climb to $275 million. Such sums would increase the budgets of the two institutes by $74 million and $18 million respectively, from the levels proposed for 1973. To offset these increases, President Nixon has recommended that about $73 million should be cut from the budget requests of all the other research institutes in the present fiscal year and that these new budget levels should be reduced by a further $43 million next year. The $73 million reduction in the budget authority of these institutes in the present fiscal year results from the cut of $11,000 million in overall federal expenditure ordered by President Nixon.

The overall picture for the research institutes of NIH is given in Table 1. The figures represent obligations not all of which will necessarily be spent in the year to which they are assigned. The situation is somewhat complicated by the fact that the appropriations bills for the Department of Health, Education and Welfare have not been passed into law because President Nixon twice vetoed HEW appropriations because he considered them to be inflationary. The totals given for 1973 therefore represent revised Administration proposals.

A large part of the cutback in 1974 funds results from the Administration's decision to phase out NIH training grants. The rationale behind this decision is that the grants were necessary to increase biomedical manpower at a time when budgets for biomedical research were increasing, but now that such budgets have been stabilized, demand for manpower will slacken off. The Administration also believes that scientists studying for PhDs will eventually earn enough money to pay back any loans they may need to finance their studies.

Table 1 Obligations for the National Institutes of Health (thousands of dollars)

Institute	1972	1973	1974
National Cancer Institute	372,838	426,093	500,000
National Heart and Lung Institute	224,389	247,075	265,000
National Institute of Dental Research	42,366	40,333	38,452
National Institute of Arthritis and Metabolic Diseases	145,032	139,806	133,608
National Institute of Neurological Diseases and Stroke	111,557	105,539	101,198
National Institute of Allergy and Infectious Diseases	103,986	100,726	98,693
National Institute of General Medical Diseases	166,358	151,587	138,573
National Institute of Child Health and Human Development	112,515	109,551	106,697
National Eye Institute	35,555	33,797	32,092
National Institute of Environmental Health Sciences	25,889	25,889	25,263
Research Resources	130,211	99,019	88,632
Fogarty Center	4,357	3,926	3,586
Total	1,457,053	1,483,341	1,531,776

So far, budgets for cancer research and for research into diseases of the heart, lungs and blood vessels have been exempted from the general budget freeze. Whether they will continue to be exempted when it becomes clear that a cure for cancer will not be found in the next few years remains to be seen.

NASA

Space Constraints

from our Washington Correspondent

FOR the second year in succession, the National Aeronautics and Space Administration has had to take a large cut in its budget and to curtail activities which, according to NASA administrator James C. Fletcher, were "important to the nation's space and aeronautics program". Most of the casualties of the squeeze were announced earlier this month (see *Nature*, **241**, 83 ; 1973), and funding for them has already been withheld from the agency's budget for 1973. As for the 1974 budget, which was unveiled last week, NASA is being allowed new starts on only two relatively small satellites, and its total outlays will decline from $3,423 million last year to $3,062 million this year and increase to $3,136 million in 1974.

As far as the Office of Space Science is concerned, the chief casualty is the High Energy Astronomy Observatory programme, which has been suspended for a review to see whether its objectives can be accomplished more cheaply. Dr Naugle, director of OSS, said last week that NASA is looking at the possibility of flying some of the HEAO experiments on an Atlas-Centaur rocket, and he hopes to have some definite plans to present to Congress during the budget hearings. The agency has, however, managed to preserve the Viking mission to make a soft landing on Mars in 1975, the two Mariner flyby missions to Jupiter and Saturn to be launched in 1977 and to keep the Explorer programme at about the same level as this year.

Funding for sounding rocket research is being held constant, at $20 million, and the only increase in NASA's physics and astronomy programme is in payload definition for the shuttle, which is budgeted at $500,000 in 1974, up from $308,000 this year. As for the planetary programmes, no approved missions have been scrapped, but there is no money in the budget for the Venus-Pioneer programme. In the middle of the negotiations between NASA officials and officials of the Office of Management and Budget, the Venus-Pioneer programme was revamped to save a total of about $50 million in the runout costs (see *Nature*, **240**, 177 ; 1972). But it seems that the ploy was unsuccessful. Asked last week whether the absence of money for the mission meant that it had been scrapped, Dr Fletcher said that NASA is still engaged in defining the programme, and hopes to get some money for it in the 1975 budget. The launch window for the first planned mission is 1977, however, which means that if it is approved, funds will have to build up rapidly.

As far as other parts of the NASA budget are concerned, the shuttle has taken a small cut, which will delay the first orbital flight by about nine months —from early 1978 to the end of that year. Skylab and the Apollo-Soyuz test project have emerged unscathed from the budget process. With Nixon's budgetary intentions now evident, NASA must be relieved that ESRO has finally decided to join the post-Apollo programme, and build the sortie laboratory.

NEWS AND VIEWS

Record Solar Activity in August 1972

DURING early August 1972, sunspot activity was responsible for a remarkable series of effects, which were observable on the solar surface, in interplanetary space and at the Earth. Three communications in this issue of *Nature* (pages 331, 333 and 335) are concerned with these events. Two are devoted to cosmic-ray studies and the third marks the advent of a new branch of solar spectroscopy at ultra-high energies.

Intense solar activity is usually associated with complex sunspot groups which in turn represent regions of enhanced solar magnetic field strength, typically several thousand gauss. Within the sunspot group a solar flare may occur; this is characterized by bursts of X-rays, optical line emission and radio waves at frequencies of the order of hundreds of MHz. Strong solar flares may emit white light for a short period and may also accelerate charged electrons and nuclei to relativistic energies, in the case of protons up to several times 10^9 eV. The nature of the acceleration process of these solar "cosmic" rays is not understood. Perhaps they are pre-accelerated in some large-scale magnetic trap by interaction with magnetic waves and only released during the flare. Alternatively the flare may reflect particle acceleration in a region where oppositely directed magnetic field lines annihilate each other and an intense electric field is set up.

More detailed angular and wavelength resolution in observations of solar activity is required to help sort out this problem, and the communication by Chupp and his colleagues (page 333) provides suitable new information on the fast protons, previously only observable when they reached the Earth or a space vehicle. Direct knowledge of the accelerated electrons comes from the radio measurements but, in the case of the protons, interaction with matter must be detected. Chupp *et al.* used a large scintillator crystal on an OSO satellite and on August 4 and 7, 1972, recorded spectral emission lines at low energy gamma-ray energies during two flares. Although preliminary measurements in this energy range date as far back as 1958 (Winckler and Peterson, *Nature*, **181**, 1317), this was the first occasion on which line emission has been detected. The lines originate from the interaction of fast protons moving downwards with matter in the atmosphere of the solar photosphere. Secondary positrons are probably responsible for a spectral line seen at 0.51 MeV, and deuterons, arising from secondary neutrons, are likely to have caused the 2.22 MeV line found by Chupp *et al.*

A companion article, by Mathews and Lanzerotti (page 335), is related to the previous work. These authors have studied the arrival at the Earth of the accelerated solar "cosmic" rays from the flare on August 7, as measured by some standard monitoring devices. By careful timing they have shown that the energetic protons must have been accelerated at the time of peak flux in the white light emission, rather than at the later time of the peak of radio and optical line emission. Thus it is thought that the white light is caused by heating of the photospheric atmosphere a few hundred kilometres above the solar surface by the downward-moving energetic protons which appeared in the acceleration process (see Svestka, *Solar Phys.*, **13**, 471; 1970).

A fast stream of plasma is ejected into interplanetary space in association with the flare activity, and it is such a stream which caused the cosmic-ray storm discussed by Pomerantz and Duggal (page 331). Interplanetary space is always filled by the expanding plasma layers of the outer solar corona and this plasma motion, at about 400 km s^{-1}, is known as the solar wind. Magnetic field is carried out from the Sun by the highly conducting plasma and is responsible for screening off some relativistic cosmic-ray nuclei from the Galaxy. The charged cosmic rays diffuse inwards, colliding with magnetic scattering centres moving outwards and losing energy as they go. The effect of the fast plasma stream linked with the flare is, however, not simply to enhance the screening process. Observations such as those of Pomerantz and Duggal show that cosmic-ray storms are made up of a series of sharp (Forbush) superimposed decreases in the cosmic-ray intensity at the Earth, often followed by a rapid recovery. Changes of intensity at the rate of 5 per cent an hour were seen in one event. And changes of particle flux are often highly dependent on direction of view. Thus it is logical to look for some large-scale barrier in space as the basis of a way to explain cosmic-ray storms.

The fast stream late on August 4, caused perhaps by a flare on August 2, reached a plasma velocity of 1,100 km s^{-1}, about the highest ever recorded by a Pioneer spacecraft. Preceding the stream was a shock front in which the magnetic field strength jumped from 30 to 40 gamma to 50 to 80 gamma (1 gamma$=10^{-5}$ gauss) according to preliminary HEOS-2 satellite data. (At quiet times the strength of the interplanetary field is no more than 6 gamma.) The shock was still very noticeable at the Pioneer on its way to Jupiter, 3.5 AU from the Sun. At the time these plasma changes were taking place the cosmic-ray intensity near the Earth is deduced to have fallen to half of its value before the storm. Only one other comparable event has been recorded, in July 1959. A theoretical explanation of the sharp cosmic-ray decreases can probably be sought either in the barrier associated with the shock jump in interplanetary field strength or, perhaps more likely, in a far-reaching plasma/field discontinuity known as a tangential discontinuity, which is expected to exist within all such interactions between the fast streams and solar wind. Magnetic field lines do not cross a tangential discontinuity, so charged particles should find it an effective barrier. Further joint analysis of satellite, space probe and cosmic-ray data for these events of August 1972 should enable a better picture of the properties of fast plasma streams ejected under flare conditions to be built up.—J. J. Q.

Crumbs from the Rich Man's Table

AT least so far as molecular biology is concerned the New Year has got off to a bright start. Much sweat has flowed under the bridge since transfer RNA was first crystallized. The incandescence of the early optimism gradually gave place to plaintive tales of unstable crystals, nonisomorphous replacements, twinning, and all the other calamities that crystallographers are heir to. Yet here suddenly come Kim and his eight colleagues from Rich's laboratory at the Massachusetts Institute of Technology, tripping down the primrose path to atomic resolution.

Success was evidently contingent, as so often in the early days of protein crystallography, on the witchcraft of good isomorphous replacement. In an article in the December issue of the *Proceedings of the National Academy of Sciences* (**69**, 3746; 1972) Kim *et al.* refer to the preparation of three heavy-atom derivatives, one containing three platinum atoms, the second two samarium and the third an osmium. It was the last that proved crucial; it involved first the preparation of a nucleotide osmic ester, from ATP and a bipyridine osmate complex. When this was diffused into the tRNA crystal it reacted stoichiometrically at a single site, the 3′ terminus, where sugar *cis* hydroxyl groups are available for complex formation. In this article a resolution of 5.5 Å was described—barely sufficient to reveal the outlines of the molecule, which was surmised only to be elongated with here and there some constrictions. The molecules are set well apart in the lattice, and in between are solvent-permeated channels. Here and there what seemed to be the phosphodiester chain could be made out, and a loop appeared to run round the outside of a part of the molecule.

Only another two months sufficed to give these shadows substance in a 4 Å model (Kim *et al.*, *Science*, **179**, 285; 1973). Here concentrations of electron density corresponding to the individual nucleotides can be discerned. The molecule resolves itself into a rough L-shape. The course of the backbone is for the most part easily traced by moving from one maximum to another the right distance away. Where the assignment is equivocal, it can be resolved by reference to the base-pairing scheme imposed by the cloverleaf model. Complete consistency between the cloverleaf scheme and the conformation in the crystal is in fact indicated, though the tertiary structure is far from cruciform. The authors are collecting data at 3 Å, which will allow them to define the structure uniquely without regard to external evidence.

It already seems, however, that there can be little doubt about the correctness of the model. The most striking feature is that there are only two lengths of double helix, each of about one turn. This means that the base-paired stems are collinear in pairs. The duplex formed by the two terminal segments of the chain is continuous with the stem of the pseudouridine loop, and is connected in the middle by way of two single-stranded segments (one of them the "extra loop") to the second double helix, made up of the base-paired stems of the dihydrouracil and the anticodon loops, the two helices lying more or less at right angles to one another. The variable length of the "extra loop", which has anything from four to twenty-one residues in the tRNA species of known sequence, can be readily accommodated, because it lies on the outside, linking the two arms of the L at their centres. Four residues in fact is the minimum length that will span the distance. The acceptor end, the 2′ hydroxyl CpCpA, projects outwards at an angle, and may be free to take up different orientations at will.

The implications of the model will have to be digested at leisure, but the authors have already noted that it accounts readily enough for various features of the chemistry, such as photodimer formation between the thiouracil residue at position 8 and cytosine at position 13. Three-dimensional models based on inferences from chemical and physical properties have, of course, dropped into the literature and vanished as rain upon the desert's dusty face; none, one may confidently predict, will survive this model. Only the base-pairing—Holley's original cloverleaf—seems unassailable. Moreover, a comparison of the X-ray data with earlier and more rudimentary results from the same laboratory on another species, formylmethionine tRNA, indicates that the gross structures must be very similar. This encourages the hope that all tRNAs will fit into the same mould structurally, just as their base-pairing schemes conform to the cloverleaf. The 3 Å model, which should yield, among other bonuses, the long-awaited proof that the base-pairing is of the Watson-Crick type (or not as the case may be), as well as a wealth of miscellaneous structural information, to illuminate accumulated experimental data, will be eagerly awaited.—From our Molecular Biology Correspondent.

Human Papova Viruses

To the numerous laboratories throughout the world that are preoccupied with cancer research the recent discovery of latent human papova viruses must come like manna. With a minimum of effort such laboratories can now submit research proposals and grant applications that surely stand a good chance of being accepted and funded. All they have to do is to propose to repeat, using human papova virus(es), the elegant and important experiments that have been carried out with simian virus 40 during the past several years. One thing seems incontestable; this new human virus is the human counterpart of SV40, a latent monkey virus that induces tumours in rodents if not in monkeys and transforms rodent cells growing in culture.

The human papova virus (whether there is just one species or several related species is not yet known) first came to light in 1971 when Gardner and her colleagues detected it in the urine of a person who had undergone kidney transplant surgery and was being treated with immunosuppressives. Subsequently the same virus or a very closely related virus was detected by Weiner and his colleagues in biopsies of brain tissue from patients with progressive multifocal leucoencephalopathy and

Weiner's group have since begun to investigate the virus by propagating it in cultured cells.

Now on page 343 of this issue of *Nature* a South African group, Lecatsas *et al.* working in Pretoria, report detecting a papova virus in the urines of no less than eight patients who had received kidney transplants. The concentration of virus in the urine and the duration of its presence apparently varied considerably from patient to patient and there was no obvious correlation between the date of detection of the virus and the date of the kidney transplantation. There may, however, be a correlation between the appearance of the virus and the use of antilymphocytic serum as an immunosuppressive. Apparently, all eight of the South Africans excreting the virus were given horse antilymphocytic serum, whereas, when working in London in 1971, Lecatsas failed to detect the virus in 150 urine samples from 31 kidney transplant patients who were not receiving antilymphocytic serum but were receiving immunosuppressive drugs. These various findings indicate, of course, that the multiplication of this latent human virus seems to depend on the immune status of an individual.

Obviously it must now be discovered whether this human papova virus(es), like SV40, has an oncogenic potential and can, for example, induce tumours in rodents and transform rodent cells in culture. From what is known about SV40 it would not be at all surprising if the human virus has an oncogenic potential. Whether, however, it is ever involved in the induction of cancer in its natural host, man, is another question. Lecatsas *et al.* propose to follow up the patients which they know have excreted the virus to see if they develop tumours and if they do whether or not the papova virus can be detected in the tumour cells, and no doubt other groups will use serological tests to see if there is any correlation between appearance of the virus and the development of tumours. But if what is known about SV40 is anything to go by nobody will be surprised if these tests all prove negative, and this human papova virus joins the ranks of other viruses which are not apparently involved in carcinogenesis in their natural hosts even though they are oncogenic in other species.—From a Correspondent.

ORGANOCHLORINE PESTICIDES

DDT Levels in Barracuda

Grossly misleading information can result from spot checking fish tissues for fat soluble pollutants in order to estimate local environmental pollution, according to the evidence of Deichmann, Cubit, MacDonald and Beasley (*Arch. Toxikol.*, **29**, 287; 1972) who have looked for organochlorine pesticides in the abdominal fat of adult barracuda shark caught in Florida waters. These pesticides enter coastal waters by terrestrial runoff and relatively large quantities of soil-bound DDT and related pesticides settle as the current decreases. As a group they are very insoluble in water, but quite soluble in fats, oils and organic solvents. DDT, as traces in solution, floating in surface films and as bottom sediment is subsequently partially absorbed by aquatic plants and marine organisms and moves through the food chain which forms the chief source of pesticide intake by fish.

Pesticide monitoring programmes have revealed that most of the fish in the waters of the United States contain DDT. They also frequently contain dieldrin, sometimes heptachlor epoxide, chlordane and heptachlor, and occasionally lindane, aldrine or endrin. Most analyses show that the "total" DDT (DDT plus its metabolites) contained in fish is less than the United States Food and Drugs Administration tolerance level of 5.0 p.p.m. for the edible portions. Concentrations of pesticide in individual tissues vary considerably; the highest concentrations are generally found in body fat. Deichmann *et al.* analysed 281 giant barracuda (*Sphyraena barracuda*); 63 per cent were found to have more than 5 g abdominal fat, and of these "fat" fish, 96 per cent contained DDT or one of its isomers or metabolites. Except for the smallest and the largest fish, the ratio of the milligram "total" DDT in fat to kilogram body weight remained constant, although the p.p.m. increased with increasing size.

Little abdominal fat was found in the barracuda with fully or nearly fully developed gonads, at the height or near the end of the spawning season (June to September). The concentration of "total" DDT was calculated in other organs and, unexpectedly, only traces were found in the ripe gonads; the fish had lost approximately 75 per cent of their "total" DDT, the female fish carrying the smaller load. Starving was not the cause of this loss of body fat plus pesticides during spawning because the stomach contents of these fish were even slightly greater than at other times. Other workers have reported high levels of pesticides in prespawning gonads, and high mortality of larvae in lake trout has been attributed to metabolization of yolk fats containing DDT. Deichmann *et al.* do not know what happens to the pesticides during the spawning season, except that they are returned to the water, to a cycle of uptake and excretion.

Two important facts emerge from this work. First, a high level of DDT in fish does not necessarily mean that greater than FDA levels will be ingested as the fat and oil containing the pesticide separate from the fish during heat-

Localization of Human *X*-Linked Genes

During the past several years cell geneticists have exploited the parasexual event of fusion of somatic cells in culture to identify linkage groups; for example, by fusing mouse and human cells and correlating the loss of human chromosomes with the loss of human enzymes from the hybrid cells it has proved possible to identify which chromosomes carry the genes for at least a few human enzymes. Obviously such experiments do not localize genetic markers to particular regions of any chromosome but, by exploiting recognizable translocations, a more precise localization of markers to particular regions of chromosomes is possible, as Ruddle and Ricciuti report in *Nature New Biology* next Wednesday (February 7).

Ruddle and Ricciuti have studied a translocation between the human *X* chromosome and the human *D*-14 chromosome detected in a mother and her mentally retarded son. Fibroblasts from these two persons were placed in culture, fused with cells of a mouse line, RAG, lacking hypoxanthine guanine phosphoribosyl transferase (HGPRT) and grown in HAT medium which selects for the retention of the human *HGPRT* gene which is *X*-linked, as are the genes for glucose-6-phosphate dehydrogenase (G6PD) and phosphoglycerate kinase (PGK).

Analyses of the pattern of segregation of these human genetic markers and the segregation of the *X* chromosome translocation led Ruddle and Ricciuti to the following conclusions. First, all these three markers are apparently located on the long arm of the *X* chromosome. Second, it seems probable that "*G6PD* and *HGPRT* are more closely linked to each other than either are to *PGK*". These experiments also prove that with patience and ingenuity somatic cell geneticists can assign markers not just to chromosomes but to particular regions of those chromosomes.

ing. An entirely different situation arises in the preparation of high protein animal feed, however, as then the whole fish is used. Second, the analysis of body fat of barracuda and similar non-migratory "fat accumulators" is a useful method of estimating local pollution, provided that year-round analyses are carried out because spot checking would lead to erroneous results.

INSECT VISION

Superposition

from our Insect Physiology Correspondent

It is now more than eighty years since Exner published his classic monograph on the optics of the compound eyes of insects and crustaceans. Exner's views have long been accepted virtually unchallenged; only in the past few years have his results been subjected to renewed critical tests, notably by G. A. Horridge and his colleagues. The classic theory of mosaic vision by the compound eye is commonly attributed to Johannes Müller, early in the nineteenth century; but it had, in fact, been put forward by Robert Hooke a century and a half earlier. According to this theory the retinal image is formed by the apposition of partial images produced by each facet of the compound eye. These partial images convey to each retinal element, or rhabdom, a stimulus characterized by their average intensity of illumination, and the resulting definition in the "apposition image" depends on the number of facets in the surface of the eye.

The most original contribution by Exner was the theory that in the eyes of nocturnal insects and some Crustacea, in the dark adapted state, the screening pigment around the optical pathway from the crystalline cone to the receptor rhabdom is withdrawn between the crystalline cones, leaving a clear zone below; and that the refractive properties of the lens cylinder, or crystalline cone, are such that light rays are deflected back towards the side from which they enter the facet, in such a way that they converge in the clear zone, and a single retinal element receives light not only from its own facet, but also light from the same point source entering through a group of neighbouring facets. The resulting image was named by Exner a superposition image. It was demonstrated most convincingly in isolated portions of the eye of the glow-worm *Lampyris*. Exner noted that the erect image so formed did not fall precisely at the level of the retina—but he suggested that this might be due to his using isolated and cleaned preparations from the eye.

Horridge first examined the eye of the firefly *Photuris* and found that no superposition image could be demonstrated. He termed the eyes with a wide gap between the crystalline cones and the receptor rhabdoms of the retina clear zone eyes (as opposed to superposition eyes, which implies a particular mode of operation.) In the meal-moth *Ephestia* there are glassy threads extending from the lens of each ommatidium to the rhabdom. These threads act as light guides which conduct most of the light received by each facet to its own rhabdom and thus a normal apposition image is produced. Furthermore, there is some scattering of light at the inner extremity of the lens and some of this reaches the retina by an indirect route. There is also a certain amount of refraction of the type described by Exner in the superposition eye—but it is too indefinite to form a useful superposition image. The eye in the dark adapted state enjoys greater general illumination but any contribution to image production must be highly diffuse.

In their most recent report, however, Horridge, Giddings and Strange (*Proc. Roy. Soc. Lond.*, **B182**, 457; 1972) show that in the skipper butterflies (Hesperidae), which are day-flying insects, there is a wide clear zone which is never interrupted by screening pigments; the pigment remains permanently between the crystalline cones even in the brightest illumination. There are glassy threads from the cones to the rhabdoms, but these are so fine that they cannot serve as wave guides for light. In the eye of these skipper butterflies the superposition principle is fully operative under all conditions of lighting and gives rise to an erect image that is tolerably sharp and is formed at the level of the receptors. Ingenious new methods were devised by which the image can actually be seen inside the eye. It would seem that although the superposition principle does not operate in all clear zone eyes, in some insects it really does exist in a highly efficient state.

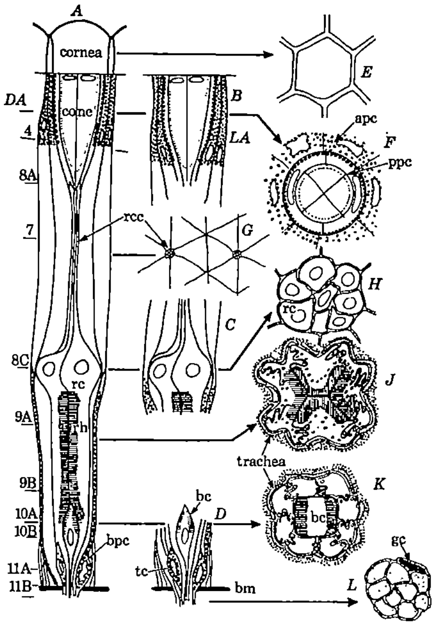


Diagram of an ommatidium, as found by electron microscopy in the skipper butterflies (figure from Horridge *et al.*, *Proc. Roy. Soc.*, **B182**, 460; 1972). *apc*, Accessory pigment cell; *bc*, basal retinula cell; *bm*, basement membrane; *bpc*, basal pigment cell; *gc*, glial cell; *ppc*, principal pigment cell; *rc*, retinula cell body; *rcc*, retinula cell column; *rh*, rhabdom; *tc*, tracheal cell.

TYMV RNA as an Amino-acid Donor

The single stranded genomic RNA of turnip yellow mosaic virus (TYMV) has some striking similarities to transfer RNAs. The structure of the 3′ end of this viral RNA apparently resembles the structure of a tRNA and the last three bases of the viral RNA are CpCpA. The ultimate A residue is metabolically labile and can be added by tRNA nucleotidyltransferase and the viral RNA can be charged with valine by valyl-tRNA synthetase. These findings prompted Haenni *et al.* to determine whether or not charged TYMV RNA can donate its valine residue to nascent polypeptide, and as they report in *Nature New Biology* next Wednesday (February 7) the viral RNA can mimic tRNA in protein synthesis.

In a protein synthesizing cell free system programmed with poly (G,U,C) valyl TYMV RNA donates its valine to polypeptide at about one-fiftieth the efficiency of valyl-tRNA. Furthermore, this reaction is blocked by puromycin and experiments with inhibitors of aminoacyl-tRNA synthetases prove that valyl TYMV RNA donates its valine directly.

In a companion report Prochiantz and Haenni describe a series of experiments which indicate that TYMV RNA is a substrate for the *Escherichia coli* endonuclease which converts tyrosine precursor tRNA to mature tRNA. This finding suggests that when valyl TYMV RNA donates its valine residue during protein synthesis the 3′ terminal portion of the TYMV RNA, which resembles tRNA, is cleaved from the rest of the viral RNA molecule.

From these results it seems plausible to speculate that the evolution of the TYMV genome has involved either the convergent evolution of a tRNA-like sequence or the attachment of a tRNA to the rest of the viral RNA molecule, an intriguing situation.

ADENOVIRUSES

Ad2 and SV40

from our Cell Biology Correspondent

WHAT renders a cell non-permissive and unable to support the replication of any particular virus is one of the more interesting questions which virologists face and no doubt the molecular basis of non-permissiveness will prove to be manifold, with different mechanisms operating against different viruses in different cells.

One of the few pertinent cell-virus combinations that has been investigated in some detail is the infection of African green monkey kidney (AGMK) cells by human adenovirus type 2 (Ad2). This virus cannot replicate efficiently in AGMK cells even though the virion penetrates the cells, is uncoated and its DNA is transcribed and replicated. When, however, Ad2 and simian virus 40 coinfect AGMK cells the yield of progeny Ad2 is increased by about 1,000-fold. Precisely how SV40 acts as a helper for the replication of Ad2 in these cells and renders them permissive remains unknown, but recent experiments carried out by Lucas and Ginsberg (*J. Virology*, **10**, 1109; 1972) seem to eliminate all but two possibilities; namely either SV40 protects some Ad2 mRNAs from partial degradation by endonucleases or SV40 specifies some function which allows late Ad2 messengers to be translated.

Lucas and Ginsberg have used DNA-RNA hybridization techniques to compare the extent of transcription of the Ad2 genome in AGMK cells, in AGMK cells coinfected with SV40 and in permissive human KB cells in which the adenovirus replicates without the aid of SV40. They also used immunological precipitation techniques to compare the amounts of adenovirus structural proteins made in these various infections. The hybridization experiments, which were carefully conducted to eliminate artefacts, reveal that both early and late species of Ad2 messengers are synthesized in KB cells and AGMK cells in the absence of SV40. Furthermore, the non-conservative maturation of these messengers and their transport to the cytoplasm are comparable in both sorts of cells. In AGMK cells, however, in the absence of SV40 the synthesis of adenovirus structural proteins is some 90-fold less than the synthesis achieved in the presence of SV40 helper. Apparently therefore AGMK cells support transcription of Ad2 DNA, but the viral RNA is not translated.

Lucas and Ginsberg do not yet know whether or not the late Ad2 messengers are partially degraded and not available for translation. If it proves that these RNAs are degraded, and they are addressing themselves to this question, SV40 must somehow protect the molecules from the endonuclease(s). If, on the other hand, the late Ad2 messengers in AGMK cells are as stable as they are in KB cells Lucas and Ginsberg will look for a function specified by SV40 that directly promotes the translation of Ad2 messengers. The result, whatever it is, will be interesting.

In the same issue of the journal (*ibid.*, 1126) Bhadani, Raskas and Green report a method for partially purifying milligram amounts of Ad2 messenger RNA from KB cells some 18 hours after infection. They have simply exploited the fact that at high ionic strengths the polyadenylic acid tails of the messengers cause them to bind to cellulose nitrate filters. As they point out, these mRNAs should prove useful for analysing the synthesis of adenovirus proteins in cell-free systems and, of course, if Lucas and Ginsberg find that the SV40 helper function is directly involved in facilitating translation, such cell-free systems may provide a means of identifying precisely the helper function.

DATING TECHNIQUES

Using Carbon–14

from a Correspondent

THE intention of the eighth international conference on radiocarbon dating, which was organized by the Royal Society of New Zealand at Lower Hutt on October 18–25, was to bring together scientists engaged in operating dating laboratories and in evaluating results. The programme was designed to deal with technical aspects of dating and the significance of isotopic ratios measured in the estimation of radiocarbon dates and with the environmental factors that might affect the interpretation of the results in terms of absolute years. It was not intended to provide a forum for the discussion of actual projects using carbon-14 dates primarily as indicators of time supporting other geochemical or archaeological evidence. The chief emphasis was on the problems of the variation of concentration and residence times of carbon-14 in ocean water; the role of radiocarbon in freshwater and in soil development; the effects and amounts of various contaminants on dates; and on considerations of suitable standards for carbon-14 activity.

It was appropriate that the meeting was held at Lower Hutt—nine miles from Wellington—because this is the site of the New Zealand Department of Scientific and Industrial Research whose director, Dr A. Rafter, with the collaboration of Dr G. J. Fergusson, established the first carbon-14 dating laboratory, with a range surpassing 55,000 years, in the Southern Hemisphere.

Of general interest were the contributions on secular variations of atmospheric radiocarbon. There are three distinct areas. Dr W. Fergusson (University of Arizona) reported that the bristlecone pine chronology had been extended by another 1,000 years to nearly 8,200 BP and that he would shortly have wood of this age available for radiocarbon analysis. Dr E. Ralph (University of Pennsylvania) and Professor P. Damon (University of Arizona) described separate methods for dealing with the nearly 400 determinations in the literature of the radiocarbon ages of dendrochronologically

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Inducing Polyoma Virus Production

IN *Nature New Biology* next Wednesday (February 7) Fogel describes further experiments with the line of rat embryo muscle cells transformed by the large plaque strain of polyoma virus which he and Sachs established in 1967. This line of transformed cells is of interest because at a frequency of about 1 in 10^4 the cells are spontaneously induced to release polyoma virus. Furthermore, various physical and chemical agents which cause DNA breakage increase the frequency of induction of virus synthesis.

In his latest experiments Fogel allowed the cells to incorporate varying amounts of 5-bromodeoxyuridine and then exposed them to various doses of visible light, a procedure which results in single strand breaks in the cell DNA. He reports that after such treatment the number of cells containing polyoma virus capsid antigen can be increased by some 600-fold and the number of cells producing virus can be increased by about 100-fold. The number of infectious virus particles produced per cell, however, decreases.

One obvious explanation of these data is that the extensive DNA breakage induced by the treatment is lethal to the cells which do not survive long enough to produce much virus. This idea is supported by the observation that exposure of the cells to cysteamine at the time of irradiation increases cell survival up to 70-fold, decreases some 2–3-fold the number of cells containing capsid antigen but increases the number of virus particles produced per cell. All these data indicate that the replication of polyoma virus in these cells is induced by single strand breakage of the cellular DNA.

dated wood, in order to provide a calibration of the radiocarbon time scale that could be used for converting conventional radiocarbon dates to calendaric dates.

It was disappointing that the conversion graphs and tables produced by the two methods did not agree sufficiently well for the conference to advise their adoption for calibration purposes. This adoption must be deferred until at least the next international conference on dating, for new data will make little difference to the curves for some time. The causes of carbon-14 variations in terms of geomagnetic and heliomagnetic cycles as well as climatic changes at the end of the last glaciation were sought as explanations by Professor A. Fairhall (University of Washington), Dr E. Ralph (University of Pennsylvania) and Dr M. Baxter (University of Glasgow). Dr Baxter warned that fluctuations induced by Sun spots could introduce uncertainties of up to 120 years in the dating of short lived materials such as grain, straw, seeds, single tree rings, twigs or egg shells.

Professor G. Östlund (University of Miami) introduced the GEOSECS oceanic programme, the purpose of which is the detailed measurement of the chemical constituents of water along sections from the Arctic to Antarctic in the Pacific and Atlantic oceans from surface to bottom. These measurements will provide a set of physical and chemical data that can be used for quantitative studies of ocean mixing and ocean productivity. They will also provide a base line for levels of pollutants and of fission and waste products being added to the sea. One of the most important sections of the programme is the measurement of carbon-14, because its half life is comparable with the time scale of mixing processes occurring in the deep ocean. Special carbon-14 laboratories are being established at Miami and Seattle (Professor M. Stuiver) to deal with the anticipated 1,200 samples each of 200 litres of water.

The nuclear bombs exploded since 1955 have doubled the radioactive carbon dioxide in the troposphere, and large doses have been injected into the lower atmosphere through the tropopause gap. All terrestrial tissues have reacted naturally to this and compounds involved in the usual processes of photosynthesis and feeding have had a fraction of all their carbon positions labelled. Mr H. S. Jansen (Institute of Nuclear Sciences, Lower Hutt) pointed out that there was now an opportunity for measuring residence times (that is, the mean time before a carbon atom residing in a tissue is replaced by atmospheric carbon) in such a way that could be expected to reflect biochemical processes in the animal or plant tissue without conducting experiments which might alter the process. He regretted the fact that the opportunity was being lost by the workers in the life sciences because the activity was at present falling by 1.5 per cent each year. He assumed that this lack of use of "bomb carbon" is probably attributable to inadequate communications between disciplines. In an attempt to redress this, Mr Jansen has compiled families of curves for various latitudes and different years of origin or birth of the tissue. He has plotted Δ^{14}C, relative radiocarbon enrichment of the tissue against calendar years so that, at a glance, a researcher can read off the rate of replacement from the curves. Other experiments can be planned with their aid.

Synthesis of Myeloma Light Chain DNA

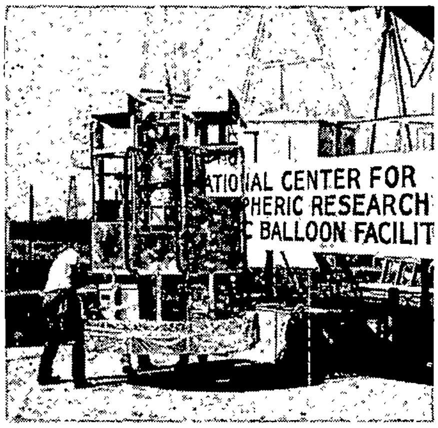
The biological role of tumour virus reverse transcriptase is apparently the synthesis of a DNA provirus during the establishment of infection, but be that as it may this enzyme in the hands of biochemists is an invaluable tool for the synthesis of DNA chains which can be labelled to a high specific activity and which are complementary to specific cellular RNA molecules. Single stranded DNA molecules complementary to at least part of globin messenger RNA molecules have recently been synthesized and partially purified, and in next Wednesday's *Nature New Biology* (February 7) Aviv, Packman, Swan, Ross and Leder report the synthesis of a DNA complementary to about 40 per cent of a mouse myeloma light chain messenger RNA.

Aviv *et al.* purified reverse transcriptase from avian myeloblastosis virus and partially purified light chain messenger RNA, which in a cell free system stimulates immunoglobulin light chain synthesis, from mouse MOPC 41 tumour cells. Using oligo (dT) as a specific primer of reverse transcription, the oligo (dT) presumably hydrogen bonds to the poly (A) residues at the 3′ terminus of the mRNA molecules, they synthesized a 5S DNA which contains about 325 nucleotides. Hybridization experiments with this DNA and polysomal RNAs from MOPC 41 cells and another line of myeloma cells, MOPC 315, indicate that the product of reverse transcription is heterogeneous.

In addition to a major species of DNA complementary to the light chain mRNA DNAs complementary to RNAs common to both MOPC 41 and MOPC 315 cells are made. As Aviv *et al.* point out, however, it should be possible to purify the major DNA species and use it to discover the number of myeloma light chain genes in these mouse MOPC 41 cells.

Two New Infrared Sources Discovered

Studies of astronomical sources in the infrared continue to be carried out by the group at University College, London. Telescopes carried on balloon flights from Texas last September scanned known objects, and also resulted in the discovery of two new sources, not previously detected in the infrared. These objects, RCW 117 and DR 15, are both HII regions, and were previously known by their radio emission.



The UCL balloon-borne infrared telescope being rigged at NCAR, Texas, shortly before launch.

Details of the observations are reported by Emerson, Jennings and Moorwood in next Monday's *Nature Physical Science* (February 5). RCW 117 appears as a compact infrared source, smaller than the 4 arc min beamwidth of the detector. It seems that it is a compact HII region, whereas the other object discussed in this work, DR 15, is not particularly compact. The new observations at infrared frequencies have made it possible to test the theory that much radiation is produced by the degradation of ultraviolet photons by dust grains. The data suggest that the amount of ultraviolet energy required could be supplied by an underlying young O star within the HII region, but that the radiation would then have to be coupled very efficiently to the dust.

EARTH'S CRUST

Velocity Inversions

from our Geomagnetism Correspondent

ALTHOUGH the so-called Conrad discontinuity is no longer recognized as a world-wide crustal boundary, the existence of more localized discontinuities in the Earth's crust is well established. During the past few years, however, evidence has been accumulating for a different, though related, crustal feature —one or more velocity inversions which effectively form low velocity layers analogous to the better-known low velocity asthenosphere in the upper mantle.

The most important of this evidence comes from large secondary P_0 refraction signals which arrive about a second later than the weaker P_g refractions at distances from several tens to at least 100 km from the shot point, although additional data are provided by normal-incidence and wide-angle observations of high-frequency intracrustal reflexions. The practical point here is that detailed interpretations of these components are now possible because of instrumental advances which have allowed the generation of broad-band recordings on magnetic tape that can be digitized and processed by digital computer. This has led to a corresponding growth in the use of the record section, comprising a series of seismograms digitally processed and plotted on a reduced time scale to permit the resolution of small velocity variations.

What has emerged from such studies is support for the existence of an upper crustal low velocity zone with a P wave velocity of about 5.5 km s^{-1} and a sharp lower boundary in the range 8–15 km. This zone is apparently not world-wide, although data compatible with it have been obtained from many continents, most frequently in areas which have been subject to major tectonic activity at some time in their geological history. The nature of the layer is not certain; but one suggestion is that it comprises semi-continuous acidic intrusions with lower densities and velocities than the surrounding country rock, and in this connexion it is interesting to note that most of the shallow earthquakes in continental areas have focal depths similar to the depths suggested for the low velocity zone. By contrast, a second low velocity layer, thought to be at depths of about 20 km beneath much of North America and Eurasia, is apparently associated with lower than normal resistivity which may be the consequence of the presence of non-meteoritic water.

As a result of the 1968 Carnegie Institution of Washington seismic experiment in the Peru-Bolivia altiplano, Ocola and Meyer (*Geophys. J.*, **30**, 199; 1972) have been able to add to this picture, first, by confirming the presence of the shallow crustal low velocity layer in that part of South America, and, second, by discovering a second low velocity zone rather deeper than 20 km. By tracing rays in a spherical Earth in such a way as to fit the characteristics of the relevant record sections, Ocola and Meyer have come up with a seismic model which agrees with the average model previously derived by Ocola *et al.* (*Earthquake Notes, Seismol. Soc. Amer.*, **42**, 3; 1971)—an upper sedimentary-metamorphic layer with a thickness of 4–9 km and a velocity of 4.5–4.9 km s^{-1}, a middle "granitic" layer down to 26–30 km and having a velocity of 6.0–6.1 km s^{-1}, and a lower "gabbroic" layer extending to 68–70 km with a velocity of 6.8–6.9 km s^{-1}.

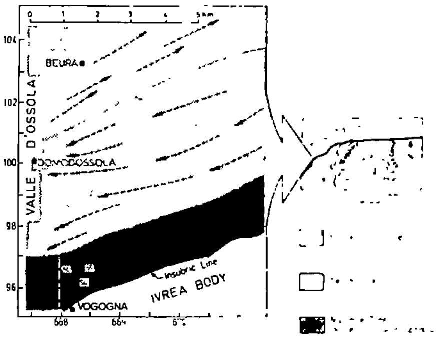
But in order to explain the large amplitudes of the secondary arrivals with apparent velocities close to those of the first arrivals, it is necessary to superimpose two low velocity layers upon this average structure. The first layer—evidence for which comes from the southern Peru record section—is the shallower and thinner of the two, has boundaries at 9 km and 12 km, possesses a velocity of 5.0 km s^{-1}, and is overlain and underlain by material having velocities of 6.0 km s^{-1} and 6.1 km s^{-1}, respectively. The deeper and thicker low velocity zone has boundaries at 30 km and 40 km (Bolivia) or 36 km and 46 km (Peru), has its own velocity of 6.15 km s^{-1}, and has material of 6.8 km s^{-1} above and 6.9 km s^{-1} below. In other words, the upper zone lies within the "granitic"

Mylonites on the Insubric Line

THE Insubric Line (sometimes called the Insubric Fault) in the Alps has been described as a late Alpine fault, the site of a Mesozoic collision trench and a post-metamorphic strike-slip fault. In short, its nature and history are subjects of disagreement, though this is perhaps hardly surprising in view of the fact that it lies in one of the most geologically complex areas of the world. Nevertheless, it is clearly a major tectonic boundary, for it forms the southern limit of high-grade Alpine metamorphism and most of the Pennine nappes, it separates radiometric age provinces and it probably forms a boundary between zones of different palaeomagnetic declination.

As a contribution to the debate on the history of the Insubric Line, Johnson reports in next Monday's *Nature Physical Science* (February 5) the results of an investigation of some of the mylonites which form part of the early section of the line outcropping west of Locarno (see diagram). This section has a character quite different from that of the later section to the east which is a clean-cut fault where mylonites, though present, are sporadic and predate the fault. The particular area studied by Johnson is the Valle d'Ossola where the Insubric Line separates the Pennine nappes from the Ivrea Body, a formation which is thought to be a slab of mantle-type material dipping towards the south-east.

Johnson is able to distinguish three episodes of deformation in the Valle d'Ossola mylonite zone—the development of the mylonite fabric from the gneisses of the Sesia Zone to the north; the development of small (amplitudes up to 30 cm) close reclined folds which deformed the mylonitic foliation; and the development of open and close crenulation folds with axial planes steeply dipping NW. The tectonite fabric of the mylonites apparently evolved during the first two of these episodes. These two episodes saw intense compression across the mylonite zone with the deformation plane lying roughly N–S. The principal axis of compression, however, which after the first deformation was oriented perpendicular to the mylonitic foliation, apparently rotated at the start of the reclined folding, though it returned to its original direction at the end of the second deformation.



But perhaps of greater importance is the orientation of the principal axis of extension. This axis is fairly steeply inclined, rather than sub-horizontal, in the area investigated by Johnson, which seems to imply that in this region the Insubric Line is not a strike-slip fault. This is why Johnson distinguished between the early and later sections of the line, because in the latter case there is definite evidence of strike-slip displacement. As for the meaning of "early" and "later", both in relation to absolute time and to the formation of the Pennine nappes, there is evidence for an early Alpine age for the deformation episodes (though a pre-Alpine age is not ruled out) and Johnson is "tempted" to correlate the deformations directly with the nappe formation.

layer of the average profile and the lower zone lies within the "gabbroic" layer.

As to causes, Ocola and Meyer also point to the question of electric resistivity (or its reciprocal, conductivity). It transpires that as a result of the "exceptional" attenuation of body waves under the Andes in southern Peru and northern Chile, discovered in 1958, various conductivity studies were actually carried out in Bolivia and Peru between 1963 and 1966 in an attempt to discover high temperature material. For example, on the basis of analyses of induced fields from both daytime and night-time magnetic variations, Schmucker *et al.* (*Carnegie Inst. Wash. Yearbook*, **65**, 11 ; 1966) concluded that a "large-scale induced subterranean jet current is guided into a high conductivity channel under the crust of the Andes", and from this and other evidence, suggested that "a highly conductive sub-stratum comes close to the surface". Later, Schmucker (in *The Application of Modern Physics to the Earth and Planetary Interiors*, Wiley, 1969) noted that the depth of this high conductivity zone would have to be less than 50 km. These findings are clearly consistent with previously discovered associations between high conductivity (low resistivity) and velocity inversions.

The low velocity zones are apparently also consistent with various geochemical-petrological conclusions drawn by Pichler and Zeil (1970, quoted by Ocola and Meyer), who suggested that the acidic and basic lavas in northern Chile and southern Bolivia derive from different parent magmas at different depths. Ocola and Meyer point out, for example, that if each low velocity layer has the same composition as its corresponding host rock but is at a higher temperature, it would be "logical" to regard the shallow low velocity zone as the source of the acidic lavas and the deeper zone as the source of the basic lavas. Thus petrochemical studies, as electrical conductivity studies, imply a higher temperature origin for the low velocity zones.

Finally, in a quite different part of the world, Bamford (*Geophys. J.*, **30**, 101 ; 1972) has also used record sections, to obtain the first evidence for a low velocity zone in the crust beneath the British Isles. The basic data in this case were obtained in the 1969 Continental Margin Refraction Experiment between Wales and Ireland ; and first arrivals have already been interpreted by Bamford (*Geophys. J.*, **24**, 213 ; 1971) in terms of a single-layer crust. But a new analysis of later refractions and reflexions indicates a 4–5 km thick low velocity layer beginning at less than 12 km and having an average P wave velocity of 5.9 km s^{-1}. Immediately below the low velocity zone the P wave velocity is 6.4 km s^{-1}, and immediately above it is 6.2–6.3 km s^{-1}. Bamford is concerned to point out, however, that these figures were obtained assuming horizontal layering and are thus only approximate.

PHYSICAL METALLURGY

How to Design an Alloy

from our Materials Science Correspondent

METALLURGISTS have dreamed of sitting down with paper, pencil and slide-rule to design an alloy ever since Henry Sorby first used the microscope to examine the fine structure of metals and alloys more than a century ago. That episode signalled the beginning of the science of physical metallurgy and more generally (for Sorby also pioneered the use of the microscope in geology) of the scientific study of microstructure.

Real life has, however, been singularly resistant to this dream. Part of the difficulty has been that so much of the really interesting detail of microstructure is below the level of resolution of the optical microscope; this objection has been removed now that the electron microscopy of thin metal films is a fully mature technique. The problem now is a theoretical one; microstructures are only statistically determinate: they cannot be described by a set of precise drawings, as can a car or a bridge. Correspondingly, the statistical theories relating, in particular, mechanical properties at different temperatures to microstructure are subtle and necessarily inexact. Overall, the physical metallurgist, as he gains in knowledge and insight, can predict the kind of alloy and the kind of treatment that will approach the desired outcome: the empirical component can never be totally exorcised.

Several case histories to illustrate the gradual improvement in the design/empiricism ratio have been assembled and analysed by Cahn (*J. Metals*, February 1973). In particular, he analyses the stages by which the Nimonics and other high-temperature alloys for jet engines came to be improved: these stages involved, alternately, advances in theory and purely experimental leaps forward. Almost simultaneously with this survey, an account has appeared of the invention (there is no other word for it) of a high temperature alloy. Berghezan and Fourdeux (*Metallography*, **5**, 485; 1972) entitled their article "The Design of Specific Microstructures in Order to Obtain Materials with Desired Properties"—an ambitious but justified title.

Briefly, what these Belgian investigators have done is to formulate a design philosophy for producing an alloy with good mechanical properties over an exceptionally wide temperature range, based partly on an accumulation of empirical knowledge concerning dispersion-hardened alloys and partly on established theory. They specify the microstructural features called for by this design philosophy, and then predict how they may be achieved. The alloy is simple enough: a 90 per cent Ni/10 per cent Al matrix is made by sintering the constituent powders, slightly oxidized. The alloy contains both some γ' phase (ordered Ni_3Al) and some finely dispersed alumina. The achievement of the desired structure is confirmed not only by conventional electron microscopy but also by the new photoemission electron microscope.

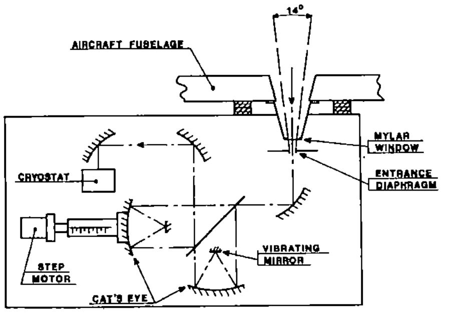
This article is not written with all the clarity one might desire, but nevertheless is both instructive and enjoyable.

Infrared Observations of the Stratosphere

OBSERVATIONS from a Caravelle aircraft which extend spectroscopic observations of the Earth's upper atmosphere to the range 25 to 200 cm^{-1} are reported in next Monday's *Nature Physical Science* (February 5). Previous studies of this kind have been restricted chiefly to the region 5 to 125 cm^{-1}.

The instrument—shown schematically in the figure—scans the sky through a 40 μm mylar window, and contains a detection element consisting of a germanium-doped bolometer at a working temperature of about 2 K. The spectra obtained show good consistency on different flights ; the most prominent features are due to H_2O rotational lines, O_2 triplets and the Q_R head branches of O_3.

Baluteau and Bussoletti, reporting this work, have also made assignments corresponding to CO, N_2O and NO transitions, because these are among the more common of the atmospheric trace gases. Some of these assignments are tentative, but there is good agreement with studies carried out at other frequencies.



Plan of the experimental system flown on the Caravelle to obtain high resolution spectra of the stratosphere between 30 and 200 cm^{-1}.

It has something of the flavour of a nineteenth century scientific paper; one has the sense of the authors thinking out some of the contributory details as they write, instead of pretending throughout, as one is apt to do, that they have magisterially foreseen everything from the start. Their metallurgical achievement, experimentally simple but conceptually subtle, is quite sufficient for them to dispense with claims to omniscience.

QUADRUPOLE COUPLINGS

Nitrogen Measured

from a Correspondent

Although nitrogen quadrupole couplings have been known for many years, a recent report by Blinc and his colleagues in Ljubljana (*J. Chem. Phys.*, **57**, 5087; 1972) demonstrates a new technique for their measurement and applies it to a number of bases such as uracil and amino-acids like cystine. When fully developed, the technique could mean much more sensitive measurements on solids. (Measurements on nitrogen-14 have always been difficult because of its small magnetic moment and the consequent weakness of the detected signals. In the 1950s Dewar used to complain that he had difficulty distinguishing genuine signals from the effects of the underground trains below Queen Mary College, London.)

The importance of nitrogen in natural organic compounds needs no stressing. But whereas n.m.r. studies on protons and carbon-13 signals are very informative, the existence of the quadrupole coupling with nitrogen-14 broadens all the resonance lines in solution and makes a simple n.m.r. experiment so unrewarding that most studies are based on the resonance of nitrogen-15, a sparse isotope with a spin of 1/2 and no quadrupole moment which usually needs enrichment. But when the nitrogen-14 quadrupole coupling can be measured in solids the results are very sensitive to chemical structure and bonding.

The quadrupole couplings depend both on the distorted, non-spherical shape of the nucleus and on the electric field gradient, which reflects the spatial distribution of the valence electrons. Results are expressed in terms of a frequency parameter, $h^{-1}eqQ$, and an asymmetry parameter, η, which measures the lack of axial symmetry. The values of $h^{-1}eqQ$ range from 0 to 7 MHz or higher, and typical of the chemical sensitivity are the values for the para diazine, pyrazine, which has $h^{-1}eqQ=4.857$ MHz and $\eta=0.536$; this differs considerably from the values for the meta compound, pyrimidine, where $h^{-1}eqQ=4.436$ MHz and $\eta=0.386$. These parameters are sensitive to environment and especially to hydrogen bonding. If the sensitivity of measurement can really be improved to the point where routine measurements are convenient, the importance for organic chemistry and biochemistry might be considerable.

The technique used by Blinc *et al.* is based on the double resonance schemes introduced by Hahn (*Phys. Rev.*, **128**, 2042; 1962; and **166**, 332; 1968). The sample spends some time in a magnetic field just large enough for the nitrogen-14 resonance, with its quadrupole contribution, to be equal in frequency to that of the protons in the same field. A flip-flop relaxation process can then operate and affect the spin level populations in such a way that any unbalance of the nitrogen-14 populations is shared with the protons. The sample then reaches a high magnetic field and the proton unbalance is examined with the high sensitivity appropriate to protons. Whether or not the nitrogen-14 populations are unbalanced depends on whether the frequency of a strong radiofrequency transmitter was or was not tuned to resonance with the quadrupole interval that is to be determined. Consequently a proton signal detector is sensitive to the nitrogen resonance.

The special importance of the particular scheme used by Blinc and his colleagues, however, is that the quadrupole resonance condition is met in zero magnetic field and so a powder or disordered solid is as useful as the single crystal required in other cases.

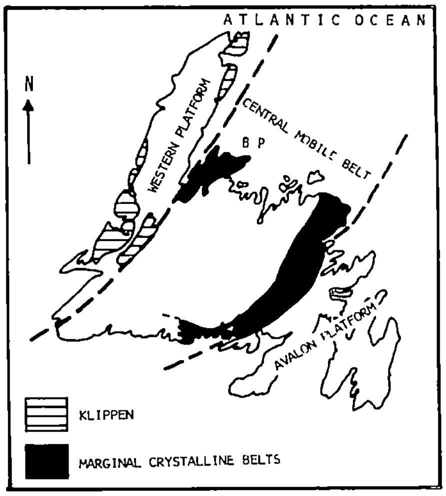
Newfoundland Ophiolites and Plate Tectonics

In next Monday's *Nature Physical Science* (February 5) the usefulness of ophiolites in unravelling pre-Mesozoic plate motions is again demonstrated, this time by Kennedy who deals with the Burlington Peninsula region of Newfoundland. The Appalachian system in Newfoundland comprises three major provinces (see diagram)—the Central Mobile Belt with its thick variably deformed late Precambrian volcanic and sedimentary rocks and, on each flank, stable platforms overlying similar rocks but which are thinner and less deformed. The Central Mobile Belt itself may then be divided threefold—an axial region which comprises chiefly Ordovician and Silurian sedimentary and volcanic rocks which are moderately deformed and incipiently metamorphosed, and two marginal belts which comprise polydeformed metavolcanic and metasedimentary rocks of pre-Ordovician age containing major recumbent folds.

The area of particular interest to Kennedy is the northwestern part of the Central Mobile Belt which, with the Western Platform, has been interpreted as a late Precambrian–early Palaeozoic continental margin. Unfortunately, as Kennedy points out, all plate tectonic interpretations carried out so far suffer from being unable to explain the pre-Ordovician polydeformation in the western marginal crystalline belt, for the ophiolite sequences in this area have usually been regarded as Lower Ordovician and so their later displacement and transport cannot be related to the polydeformation.

From a reinterpretation of the structural relationships in the western marginal crystalline belt, Kennedy concludes that there are two ophiolite sequences of different ages; thus although one is undoubtedly Lower Ordovician, as previously thought, the other is pre-Ordovician. The older sequence is structurally complex, apparently lacking the simple characteristic ophiolite structure, and is interpreted as the remains of a small ocean basin which closed and had its ophiolites obducted before the Ordovician. The polydeformation is then taken to reflect periodic movements in the closure-obduction process. All this predates the formation of the second sequence of ophiolites which were presumably produced by later seafloor spreading and thrust up to their present position by later obduction. In this case no ocean basin closure was involved and so there was no transmission of stress through the adjacent rocks and hence no deformation.

In this way Kennedy is neatly able to solve a local problem. As he points out, however, the solution is really of more than local importance because "it provides the basis for relating some metamorphic nappe complexes in linear orogenic belts to plate movements".



The tectonostratigraphic divisions of Newfoundland. BP, Burlington Peninsula.

SOLAR SYSTEM

Celebrating the Birth of Copernicus

by our Astronomy Correspondent

IT is fortunate for the organizers of celebratory conferences that the quincentenary of the birth of Copernicus comes at a time when the study of the solar system and planets is in a healthier state than ever before, even though the end of the Apollo programme has left many selenologists less cheery than is seemly for scientists with so much unanalysed data still up their sleeves. After all, only a few weeks ago an article in *Science* reported the bemoanings of staff at the Manned Spacecraft Center, who apparently have more lunar material than they know what to do with. Had the Copernicus quincentenary occurred only fourteen years ago, before the Lunik flights that is, the celebratory symposium held by the Royal Society and the Royal Astronomical Society in London last week would have dealt with the work of a few dedicated scientists, far removed from the modish astronomy of the day, struggling to glean what they could by peering at objects which from the Earth are only a few seconds of arc in diameter (for example, Mars, 25 arc s) or at best 30 minutes of arc in diameter (the Moon).

Things are different now, as Professor S. K. Runcorn (University of Newcastle upon Tyne) made clear in his review of knowledge of the Moon, which was founded for the most part on information which has come from the Apollo missions and the preceding Orbiter series of automatic lunar satellites (the Orbiters relayed back to the Earth enough detailed photographs of the Moon to keep selenologists busy for years). For example, Professor Runcorn suggested that the moonquakes which have been identified by the seismic network on the Moon as occurring at the edges of the circular maria may arise as a result of the slow sinking of material into the Moon at these locations. According to Professor Runcorn, the existence of this slowly-settling material is suggested by the presence of the gravity anomalies at the circular maria (the mascons, identified by analysis of the motions of Orbiter spacecraft). He suggested that these mascons arise after the circular mare basin has been punched out of the surface by the impact of a meteorite, and after the basin has been filled with lava from below. The solidification of the lava pool leads to a fall in the level of the surface by about 2 km, and it is the further molten material which has welled up from below to fill this 2 km which is the cause of the anomalous gravity, while the gradual sinking of this circular plug of material gives rise to some of the moonquakes.

But Professor Runcorn could offer no evidence bearing on the question of the origin of the Moon, which, he said, is still largely a matter of taste, although he prefers the view that the Moon accreted from a cloud of dust around the Earth.

Venus and Mars were dealt with by Professor R. Goody (Harvard University) who said that some kind of consensus is now emerging on several topics to do with these planets as a result of the American and Soviet space programmes, ground-based observations, and theoretical work by geophysicists. He said that the investment in this work of a small proportion of the budgets of the American, Soviet and European space programmes will ensure continuing revolutionary discoveries.

Compared with the Earth, Mars and probably also Venus are gravitationally rough, indicating the existence of strong tectonic processes. Professor Goody recited the important discoveries on Mars made by Mariner 9, which include the largest volcano in the solar system (Nix Olympica, which seems to be at least 10 km high, and perhaps even higher), an enormous canyon with dendritic features (Coprates, which among other reasons is odd because there is no sign of any debris which might have been expected to be left behind), and features resembling desert washes which must have arisen by the flow of a liquid over the Martian planes.

The cameras also snapped one of the Martian moons, Phobos, which, of course, can have no atmosphere or internal processes to wipe its surface clean of craters because of its small size. Its crater density, a hundred times that of the Martian surface in general, should therefore be a useful calibration mark for studies in which the ages of Martian surface features are estimated from the density of craters.

As a meteorologist, Professor Goody was obviously not too disturbed by the dust storm which at first hid the Martian surface from the cameras. He conjectured that a mechanism not unlike that of a tropical hurricane could pump the atmosphere of Mars full of dust in a matter of days, and said that some of the photographs towards the end of the storm show features reminiscent of a terrestrial cold front. Professor Goody concludes from his study of the Martian atmosphere that seas might have existed there at an earlier epoch, so that Mars ought to be examined for fossils.

Jupiter and Saturn have not been studied by space probes, although Pioneer 10 is now across the asteroid belt and should reach Jupiter toward the end of this year, so Professor R. Hide (Meteorological Office) was limited to ground-based information in his talk, although the radio emission from Jupiter is a useful phenomenon which no other planet can match. It seems that the emission can be divided into three classes—thermal emission from the disk, decimetre radiation which comes from an area much larger than the disk and is assumed to have a synchrotron origin, and decametre radiation which appears in bursts apparently controlled by the position of the satellite Io and which comes from areas much smaller than the disk.

Professor Hide is also a meteorologist and much of his talk was a discussion of the atmospheres of Jupiter and Saturn, in particular the Red Spot of Jupiter which has a history going back three centuries, whereas with other similar-sized features in the Jovian atmosphere seem to come and go in a matter of weeks. Professor Hide still seems to favour the view that the Red Spot is a Taylor column depending for its existence on an interaction between the atmosphere and some kind of feature on the surface of the planet (or between the atmosphere and a solid object floating in it).

Copernicus's own field of planetary motions was discussed by Dr G. A. Wilkins (HM Nautical Almanac Office). In particular Dr Wilkins discussed the strange relations which occur between the periods of the outer planets, and between the periods of their satellites. For example, five periods of Jupiter are equal to 2.013 periods of Saturn, three periods of Saturn equal 1.052 periods of Uranus, and two periods of Uranus equal 1.020 periods of Neptune. Similar commensurabilities occur among the satellites of Jupiter and Saturn (indeed, in the case of Saturn the relations extend to some features of the ring system). A full explanation of these phenomena is still not available—questions such as how the regularities arose, and whether they strengthen the system or will eventually lead to the system breaking up, need to be answered—but it seems that tidal friction must be the chief mechanism.

Dr Wilkins also discussed Ovenden's "Principle of Least Interaction Action" by means of which Ovenden has come to some conclusions about the nature of a missing planet in the asteroid belt (*Nature*, **239**, 508 ; 1972), and although the full details have yet to be published Dr Wilkins feels that Ovenden's principle may turn out to be useful in planetary mechanics.

The AEC and the Loss of Coolant Accident

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Professor Wilson gives the background to the concern being expressed about the risks associated with the possible loss of coolant from a nuclear reactor.

ONE of the chief worries associated with a nuclear power station is the possible accidental release of large quantities of radioactivity. The fact that part of the energy release is in the form of radioactivity creates a unique hazard, which can exist even in the absence of an explosion. This radioactivity persists long after the nuclear fission has taken place; Fig. 1 shows the fission product radioactivity produced by a typical nuclear power station after running for an infinite time at 1,000 MW (electrical) (=3,000 MW (thermal)). Immediately after switching off, the power is still 250 MW, and there is 10,000 million curies (Ci) of radioactivity. Under ordinary circumstances it is obvious that this radioactivity is contained, for nuclear power stations actually exist. Although some release nearly 10^6 Ci a year, radiation doses near them are measured to be small. But the accident problem remains.

It now seems probable that the worst possible accident from the point of view of the exposure of the public to radiation is not a runaway nuclear reaction, but a loss of reactor coolant accident (LOCA), which has received much public attention recently in the United States. The purpose of this article is to illuminate the technical problems, although more lengthy reviews are now available[1].

All nuclear power stations at present operate as steam generating power stations. The higher the temperature of the steam the greater the efficiency. A typical nuclear power plant operates with steam at 600 K, and gives a theoretical Carnot cycle efficiency of 50 per cent and a practical efficiency (using a Rankine cycle) of about 33 per cent. At this temperature water is at a high pressure in the boiler. In the reactors cooled and moderated by water, the reactor vessel must also be at this pressure.

This means that a catastrophic accident could take place if a failure occurs in the reactor vessel or steam piping. The water/steam mixture would leave the reactor (blowdown); even if the break were above the reactor vessel the superheated water would mostly boil away leaving the core uncooled. The nuclear reaction would cease as soon as the moderator disappeared, but Fig. 1 shows that heat would still be produced at a rate of 250 MW in a typical reactor core of 1,000 foot[3].

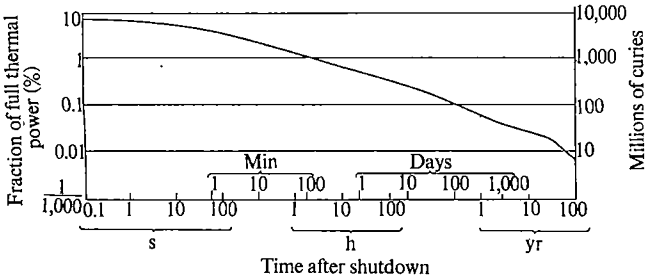

Fig. 1 Radioactivity and fraction of full power from infinite irradiation in a large reactor of 1,000 MWe.

If no steps were taken to re-establish core cooling, the core would melt. The subsequent course is unclear. An Atomic Energy Commission task force outlined in 1967[2] several possibilities. In a few minutes the molten core would fall to the bottom of the reactor vessel; in half an hour it would melt the 6-inch thick steel vessel; in a day or two it would melt through the concrete "secondary containment" vessel; finally (in about three months) it would solidify several hundred foot underground. This is, for obvious reasons, called (in the West) the China syndrome. No one knows what would happen to the radioactive fission products, a quarter of which—xenon, krypton and iodine—are gaseous and would certainly not be contained by a molten ball of liquid, although the "secondary" containment might be intact. If cooling is attempted after meltdown has occurred, various mechanisms can be postulated by which the uranium, with even the non-gaseous fission products such as strontium-90, could be spattered over the power station and maybe over the countryside too. The course of events after such a release of radioactivity is also uncertain[3–5]. Under favourable meteorological conditions no one would be hurt; under unfavourable ones, a wind of 6.5 m.p.h. with a temperature inversion, the radioactivity would stay close to the ground and thousands of people could die. Fortunately some hours are available to allow evacuation, which is more warning than for a large earthquake, tidal wave or dam failure.

It is hard to predict the likelihood of failure of a steam system. The reactor vessel itself is six inches thick and it is believed, but not absolutely proved, that it could not fail catastrophically; connecting pipes of diameter up to 30 inches could, however, fail. Accordingly, all the reactor safety criteria specify the best materials for the reactor vessel and pipe. The welds in the pipe are X-rayed and tested ultrasonically; moisture detectors are used to detect small leaks before they enlarge to become dangerous breaks.

Catastrophic breaks have occurred in other places, like laundries and fossil fuel plants, where steam pipe of lesser quality is used under pressure. There is no publicly available listing of such failures, which is an omission on the part of nuclear industry and of the AEC. I would guess the failure probability to be less than 1 in 1,000 power station years for "ordinary" pipe, and 1 in 10,000 for "reactor grade" pipe. As 500 nuclear power stations are projected for the year 2000, this would still be a failure every 20 years, which is too large. Accordingly, emergency core cooling systems (ECCS) are built to re-establish cooling as soon as possible in the event of loss of coolant. These ECCS devices do not depend upon the automatic action of a law of physics but are engineered safeguards and depend upon the reliability of the engineering. This feature already makes critics nervous—especially those critics who, like myself, have problems in making gadgets work.

In the event of a small break in water piping, pumps start and resupply water very quickly. It is the large break

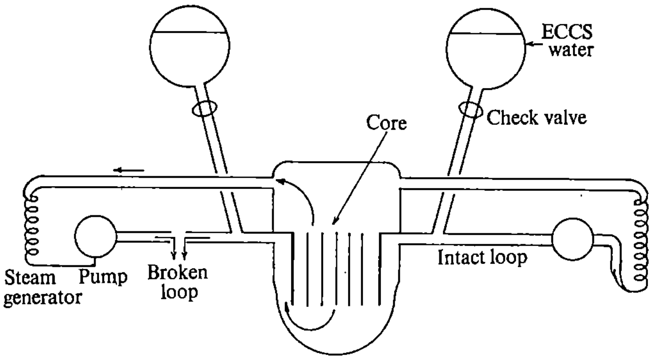

Fig. 2 A schematic drawing of a two-loop PWR showing steam/water mixture leaving a double-ended guillotine break, illustrating flow stagnation in the centre of the core.

that is the problem, and the AEC design criteria assume that on-site power is lost simultaneously with the accident, and that emergency diesel generators must be used. The diesel generators can start and take load in 25 s, and 30 s is assumed. This is not considered to be fast enough for pressurized water reactors (PWR), and large pressurized water tanks (accumulators) are available to inject water (borated to inhibit a nuclear reaction) as soon as the pressure falls sufficiently to allow a check valve to open.

Fig. 2 shows the details of the cooling system of a PWR, which is the type of reactor most subject to criticism. Hot pressurized water passes from the top of the core, through a heat exchanger (steam generator), through a pump, and back to the bottom of the core. The core is made up of 36,000 fuel rods, each 16 foot long and 0.5 inch in diameter, in an open arrangement of 16×16 bundles. The rods are zirconium alloy (zircalloy) tubes filled with pellets of uranium dioxide (UO_2) ceramic. Initially the zircalloy "cladding" has the temperature of the coolant, 600 K. Because it reduces capital expense to use a compact core, the centre of the fuel in the hottest rods is run at as high a temperature as possible—2,500 K—which is just below the melting point of UO_2.

In a LOCA, the steam/water mixture leaving the core may cool the core for some seconds. During this time the heat stored in the UO_2 will be transferred by conduction to the cladding and removed. But in a PWR it is possible, as illustrated, to envisage a break in such a place that steam leaves the core from both top and bottom, leaving a stagnation point in the middle of the core where there is no flow. If this stagnation point were to be established at the hottest point in the core, the temperature would rise to about 1,400 K before the inside and outside fuel temperatures would be equalized, and after that would rise at 10 K a second because of decay heat.

Elaborate computer programs have been written to describe this blowdown in detail, and, as shown in Fig. 3, these predict flow oscillations and appreciable cooling[6]. There are two coupled parts to the program: the evaluation of the core flow, and the heat transfer. Both have been compared with model tests, but for theoretical reasons the heat transfer coefficients are in doubt. In ordinary operation, heat can be transferred to the water by nucleate boiling, as applies, for example, to a pan of boiling water. Heat is removed very rapidly by this method. But if water is brought to a hot, dry, vertical surface, film boiling can occur in which a steam film forms, through which heat must then be transferred—for this type of boiling, the heat transfer coefficient is 10,000 times smaller. Moreover, heat transfer coefficients are derived from small-scale measurements, and it is not completely clear how these may transform to large-scale geometries. Therefore, if a stagnation point can occur, even for a fraction of a second, it is prudent—and required by the AEC—to assume an immediate switch to the lower heat transfer coefficient for film boiling.

This large change in heat transfer coefficient leads to problems in experimental determination of the coefficients. Neither type of boiling is calculable theoretically. It is, however, believed that heat transfer is dependent on fluid flow and quality (amount of steam) through dimensionless parameters such as Reynold's number and Prandtl's number, and only implicitly dependent on the geometry. The experiments use a few rods in simple geometries, and it is hard to be sure that film boiling is achieved, for any turbulence can lead to rewetting of the surfaces, with a consequent rapid increase of heat transfer. This might indicate that experimental numbers should be used whether or not film boiling is achieved; critics argue, however, that in larger geometries the fluid might preferentially avoid the "hot spot", leading to stagnation. Therefore, although all model tests so far indicate excellent cooling during blowdown[7], this may mean nothing for a reactor.

The computer programs could be checked by blowdown measurements on a large reactor. Accordingly, in 1963 the loss of fluid test (LOFT) reactor was begun by the Idaho Nuclear Corporation (now Aerojet Nuclear Corporation) for the AEC. This large scale test is seriously delayed and will not be ready until 1975. Meanwhile, there are partially scale systems tests which examine parts of the phenomena.

When the blowdown is in progress, water injected into

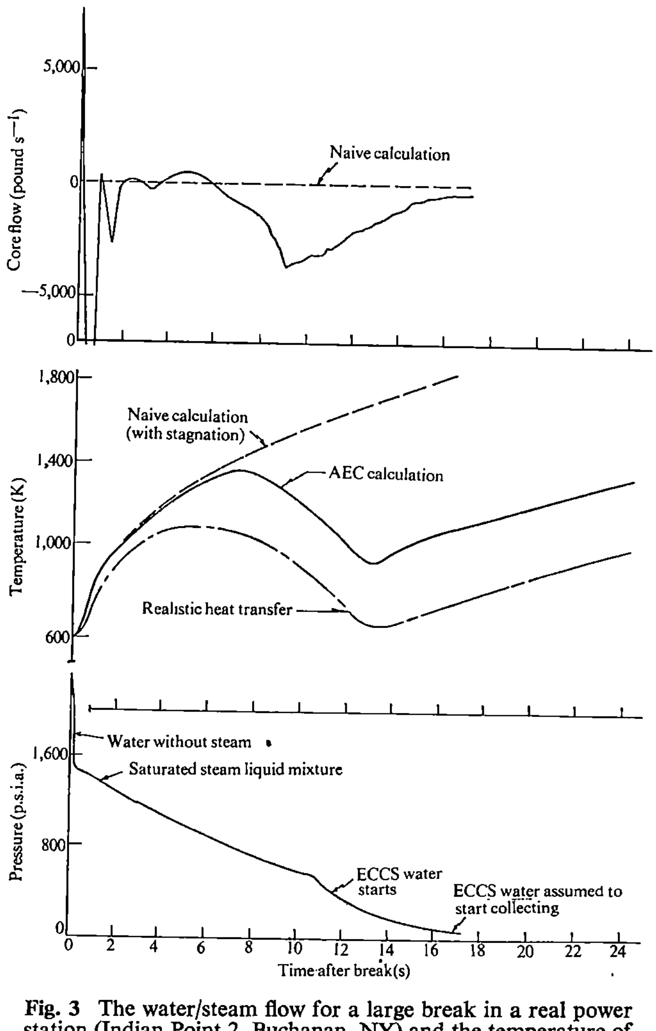

Fig. 3 The water/steam flow for a large break in a real power station (Indian Point 2, Buchanan, NY) and the temperature of the hottest spot in the core calculated using AEC approved heat transfer coefficients. Note the predicted heat removal during blowdown.

the reactor vessel might be hindered by the outgoing steam (steam binding). In "semi-scale" tests (about a tenth the size of a real reactor) water failed, however, to stay in the test vessel although cooling of the electrically heated test rods was good[8]. This rejection of the emergency coolant was unexpected and alarming; the reactor manufacturers' computer programs explained this result after the event, and they say that it will not happen in a real reactor. But the interim AEC regulations insist that it be assumed that no water stays until the blowdown is over (the steam flow stops).

As the incoming water meets the hot zircalloy surfaces, steam will be produced. This steam must escape from the reactor, and it will carry with it entrained droplets of water, reducing the filling rate. There are two paths for the escape of steam; one through the broken loop—direct to the break—and the other through the intact loop, past the incoming ECCS water injection to the bottom of the reactor and from there to the break. The resistance to steam flow can reduce the injection somewhat, particularly if the incoming water "plugs" one of the pipes. The filling rates were measured in a set of tests of small rod assemblies (Full Length Emergency Core Heat Transfer or FLECHT tests) which were difficult to perform because of the high temperatures involved and were not very precise. Some scale tests on pipe plugging are commercial secrets; a few tests have been carried out on steam binding but none in a large reactor.

Another problem, which is probably less serious, arises from the effects of high temperatures on the zircalloy fuel cladding. During the blowdown the heated zirconium cladding will heat, expand and finally burst because of internal pressure at temperatures between 1,000 K and 1,300 K[9]. These bulging tubes can block coolant flow, but no one knows for sure how much, for the core has an open structure and water should be able to get around. Moreover Fig. 4 shows that there are control rod tubes which stay cold.

These uncertainties would be unimportant if the temperature in a LOCA could safely reach the melting point of the ceramic UO_2 at 2,950 K, or even the melting point of zircalloy at 2,100 K; then the rods could lose heat to each other and to the cold parts of the vessel by radiation—which varies as T^4. But zircalloy has an exothermic reaction with steam, which becomes important above 1,200 K. Above 1,900 K cooling water heats up the cladding instead of cooling it, and oxidizes it. Oxidized cladding becomes brittle on cooling, and can collapse causing more drastic blockages to flow. This happens particularly rapidly if the cladding has expanded, or if steam gets to both sides of a burst tube.

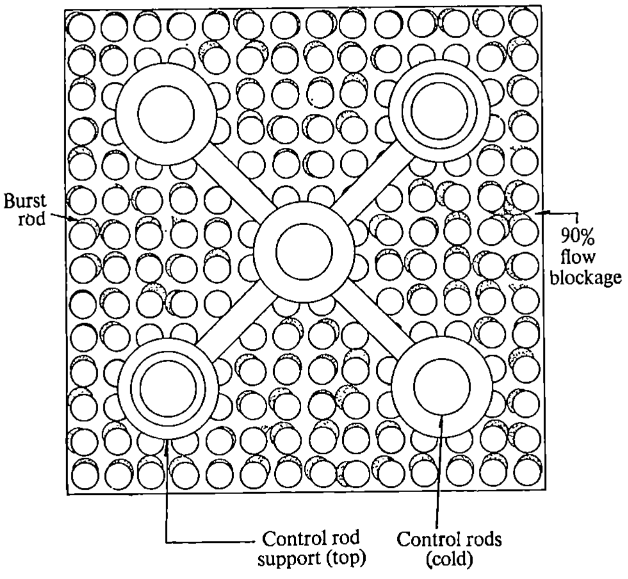

Fig. 4 A section through a PWR fuel bundle, showing spaces for control rods, and possible flow blockage.

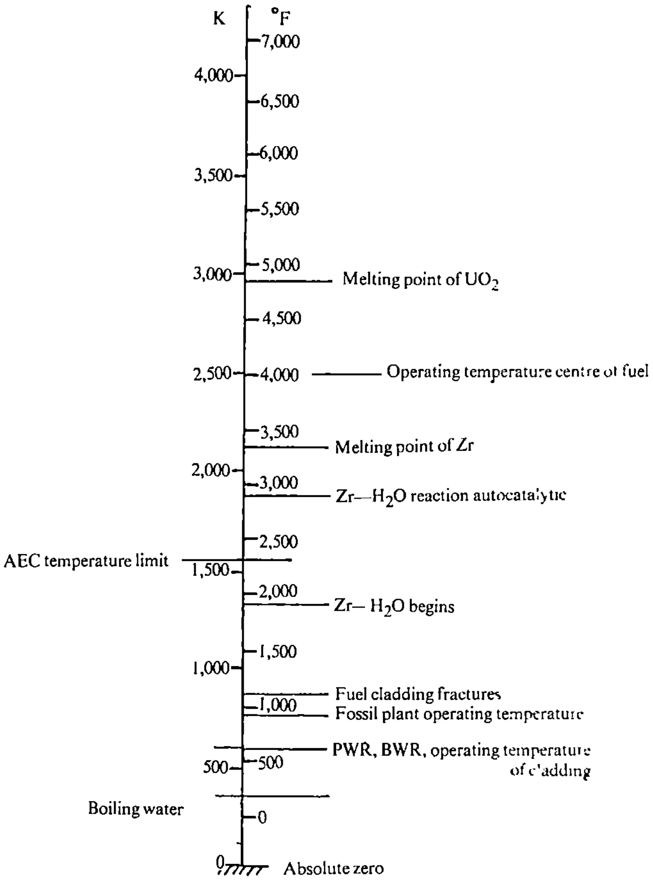

Fig. 5 Critical temperatures in reactor operation.

If a reactor were operated at a low power level, say 60 per cent of current designs, the uranium temperature would be lower and the heat stored in the core much lower, particularly as the specific heat of UO_2 ceramic rises with temperature. It is easy to show that ECCS water would be adequate even if no heat were removed during blowdown; at the lower power, steam binding would also be less important.

In 1971 some critics outside the AEC[10] and some inside it[11] recommended that the large reactors coming up for licensing should be restricted to a low power level until the LOFT tests are performed. This would be more logical than a complete moratorium proposed by others[12]. The AEC chose to restrict reactors less than this, and in June 1971[13] promulgated interim acceptance criteria for emergency core cooling systems. These limited the calculated temperature to 1,600 K with supposedly conservative heat transfer coefficients and power distribution.

So began a series of procedural errors by the AEC. The interim criteria were not accompanied by an explanatory white paper. Industry, who make both the problems and the profits, did not help. The PWR manufacturers keep even their safety information proprietary to get an edge on their competitors and not even a non-proprietary version of their report[14] was available for six months[15,16].

Critics, both friendly and unfriendly, felt that a central public hearing was necessary to enable the best talent to discuss this question instead of having it discussed with inferior talent at every separate hearing for a power station licence[17]. The AEC agreed to a hearing in November 1971 and finally presented its written hearing testimony in December 1971. In doing so, the AEC made two more mistakes. Already, on June 30, 1971, the budget of two of the AEC's reactor safety research laboratories had been cut following the desire of Congress to "force" the reactor vendors to pay for safety research. These laboratories, Oak Ridge National Laboratory and Aerojet Nuclear Corporation, act as devil's advocates for the AEC in its dual role of promoting and regulating the nuclear industry. Next they were asked to change their roles and to defend the AEC's interim criteria. As anyone should have expected, their testimony raised all the criticisms noted above, and tended to suggest that the budget reductions were foolish, and that their role as critics is vital.

A logical procedure for safety hearings might be for the reactor vendors (who design the ECCS systems) to present the case that reactors are safe; the AEC's devil's advocates could criticize and demand proof at every stage, with aid from the concerned public (now grouped in the Consolidated National Intervenors) and the AEC's regulatory staff could have been waiting in the middle—as indeed they had been the previous year when these arguments were going on in private. Instead, the AEC's interim criteria were made the subject of the hearings, thus destroying whatever logic had been present in the AEC's administrative stance.

During the first two months of the hearing (February and March 1972) the lawyer for the Consolidated National Intervenors (Mr Myron Cherry), aided by a young economist from Harvard (Daniel Ford), with MIT physics professor Henry Kendall in the background, tried to prove that these criteria are arbitrary and capricious; an easy task since regulations are, by their nature, arbitrary. They found inevitable disagreements between a hundred witnesses from the AEC staff, ORNL and ANC. P. Rittenhouse of ORNL wants to replace the simple temperature limit of 1,600 K by a calculation of oxidation and embrittlement and Dr L. Ybbarrondo of ANC believes that the heat transfer coefficients may not be adequately conservative, and blowdown flow rates may be lower than calculated in the region of the hot spot.

During the summer, the reactor vendors and intervenors presented testimony on which they were cross-examined, and rebuttal testimony was presented in October 1972. Meanwhile the trend towards higher power per unit length in the reactors is halted. The General Electric Company make a boiling water reactor (BWR) whose internal circuits make it less liable to flow stagnation and therefore less liable to criticism. Nonetheless GE have announced a new fuel element of smaller size (seven-eighths of the former). This new fuel element will store less heat; it was designed primarily to prevent cracking at high temperature (as happened at the Dresden II power station in Illinois), but it also will keep down the temperature in a calculated LOCA to 1,100 K—a level which the critics may find acceptable. The fuel fabrication cost is roughly proportional to the number of fuel rods and increases 30%. But it only represents an increase of 2% in the total cost of nuclear power. Westinghouse have also announced a fuel element of smaller size to increase the margin of safety.

In May 1972 (ref. 18) serious defects were discovered in nuclear fuel made by Westinghouse. In three large reactors, BEZNAU, Switzerland; GINNA, New York; and ROBINSON No. 2, N. Carolina, voids have occurred between uranium pellets, and zircalloy tubes (which are susceptible to creep) have collapsed because of the external pressure, like a squeezed toothpaste tube. A collapsed tube leaves more moderator at the point of collapse and this gives a very peaked power distribution with a hotter "hot spot" in a LOCA. Some of these tubes have leaked, but it is feared that many might leak simultaneously with a consequently large radioactivity release. No one knows for sure why the voids appear between the pellets; the pellets are made of sintered UO_2 of less than the maximum density and they seem to become denser (and shrink) on irradiation. Or the voids might be a consequence of careless manufacture.

The present Atomic Energy Commission chairman, James Schlesinger, is more sensitive to criticisms than his predecessor. The AEC regulatory staff insists that all PWRs with zircalloy fuel operate at reduced power to make up for possible power peaking and possible increased brittleness of the cladding. The General Electric BWR uses a lower pressure and thicker clad and shows no such problem; the other manufacturers must prove that this problem does not occur. Combustion Engineering use thicker clad and denser fuel than Westinghouse, and X-ray each fuel rod to prove the initial absence of voids, but their two reactors are still held at low power pending better proof. Some utility companies are now proposing operating conditions with reduced power peaking and hence greater safety margins.

Such changes may increase the cost of nuclear power stations. If the reactor vendors are right, the reactors are already safe, but it will be more obvious that they are safe. Until recently, nuclear proponents feared that unnecessary cost increases would price nuclear power out of the market, causing more fossil fuel to be burnt with much more air pollution and its attendant death toll. But cost will not now stop nuclear power. Recently the east coast cities in the United States demanded that utilities burn oil of low sulphur content to avoid SO_2 emission; natural gas is not to be had. Because of this the price of fuel oil has risen three-fold (from $1.75 to $4.75 a 42-gallon barrel in Boston) in two years. Interest on a high capital cost is less than a high, and increasing, fuel cost.

This increase in fossil fuel prices is likely to continue all over the world as fuel reserves run short. In Britain, for example, the Central Electricity Generating Board has announced that three of the Magnox reactors produced the cheapest electricity last year. This was in spite of the power reduction ordered following the discovery of corrosion of the Magnox fuel in one of these reactors. A similar, temporary power reduction in the United States would have a similar, temporary, and small effect.

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Function of Lipophilic Acids as Antimicrobial Food Additives

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Most antimicrobial food additives are lipophilic acids which prevent growth by inhibiting the transport of substrate molecules into cells. The inhibition of transport was also observed in membrane vesicles, even when they were derived from organisms for which growth and transport are not affected by the larger inhibitors.

MOST antimicrobial food additives (preservatives, Table 1) now in use are lipophilic acids which inhibit the growth of unwanted microorganisms, usually without killing them (exceptions are alkylating agents). They are ingested in significant quantities but do not grossly interfere with the human organ function as judged by toxicity tests. So far their inhibitory mechanism remained unknown[2]. We wish to show here that it results from the inhibition of substrate transport into cells.

Inhibition of Microbial Growth

Preservatives are weak acids whose growth inhibitory effect increases when the *p*H is lowered from neutrality (except for parabens, with a *p*K above 8), indicating that inhibition results from the undissociated acid[2,3] (whose fraction can be calculated from the known *p*K values, Table 1).

As the inhibitory concentrations of compounds differ greatly, the inhibition index is plotted against the logarithm of the inhibitor concentration in Figs. 1–3. (Index=0 if there is no inhibition and 1 if there is no growth. Values above 1 signify cell lysis.) The concentration of fatty acids (Fig. 1*a*) or parabens (Fig. 2*a*) needed to produce a certain amount of growth inhibition of *Bacillus subtilis* (at *p*H 6.5) decreases with increasing chain length[3], saturated and unsaturated fatty acids being about equally effective. Presumably, the more lipophilic long chain compounds are more effectively partitioned into the cell membrane. This membrane attachment is reversible, because when cells, inhibited by fatty acids from acetic to linoleic acid or by propylparaben, are resuspended in fresh medium, growth resumes immediately at the uninhibited rate. Fig. 3*a* shows that sulphite, nitrite and benzoate inhibit efficiently, while nitrate has almost no effect. 2,4-Dinitrophenol (DNP) is as effective as long chain fatty acids. The antioxidants ascorbate and erythorbate inhibit only at high concentrations.

Inhibition by fatty acids (Fig. 1*a*), DNP and sulphite (Fig. 3*a*) increases about ten-fold (from 0.1 to 1) when their concentration is raised by a factor of 10, indicating an essentially linear concentration dependence. The increase is more rapid for the parabens (Fig. 2*a*) or nitrite (Fig. 3*a*).

Fatty acids and propyl parabens inhibit the growth of *B. pumilis*, a close relative of *B. subtilis*, to the same extent (Figs. 1*a* and 2*a*). Strains of *B. subtilis* or *B. pumilis* (renamed) produce "rope" in bread, a spoilage which is prevented by the inclusion of propionate[2,7].

Mechanism of Inhibition

Compounds which inhibit the polymerization of RNA (actinomycin D) or protein (chloramphenicol) do not inhibit cellular oxygen consumption, while the preservatives do (Table 2). Because *B. subtilis* is strictly aerobic this inhibition entails the depletion of ATP, the concentration of which is reduced by up to 90% (Table 2)[5].

Although saturated fatty acids inhibit cellular oxygen consumption, they do not inhibit the NADH oxidation by isolated membranes (Table 2)[8], that is by the cytochrome-linked electron transport system[6]. Therefore, the inhibition of oxygen consumption in whole cells must result from the deficiency of compounds that enter electrons into the electron transport chain. We will show below that this deficiency results from the inhibition of transport of the necessary substrates into cells. Saturated fatty acids inhibit the uptake of serine or α-amino-isobutyric acid in *B. subtilis*[8], and the uptake of arsenate or phosphate in yeast[9,10]. Inhibition of cellular

Table 1 Common Food Additives

Antimicrobial food additives*	*p*K†	Maximal millimolal concentration present in certain foods‡ mmol kg^{-1}	Food
Acetate, C_2 (H, Na, K; di-)	4.76	500	Pickled food
Benzoate (H, Na)	4.2	8	Beverages
Heptyl paraben§	8.47	?	Beer
Methyl paraben	8.47	5	Beverages, jams
Nitrite (Na, K)	3.29	3	Meat
Octanoate, C_8 (caprylate)	4.88	?	Cheese wrappers
Propionate, C_3 (Na, Ca)	4.87	100	Cheese
Propyl paraben	8.47	0.6	Creams, pastes
Sorbate (H, K, Na)	4.8	30	Cheese
Sulphite (mono-, bi-; K, Na; SO_2)	1.8, 7.0	5	Wine

Other compounds used (*p*K values in parentheses): ascorbate (4.19, 11.57); benzoate (4.20); *n*-butyrate, C_4 (4.82); *n*-decanoate, C_{10}=caprate (4.9); 2,4-dinitrophenol, DNP (4.1); erythorbate=isoascorbate; ethyl-paraben (8.47); *n*-hexanoate=caproate, C_6 (4.87); *p*-hydroxybenzoate (4.58, 9.31); linoleate, C_{18} (4.9).

* In parentheses are listed the cations with which the compounds are usually added or alternative forms or names of the compounds.

† Data from Jencks and Regenstein[1].

‡ Data calculated from values given by Chichester and Tanner[2].

§ "Parabens" are esters of *p*-hydroxybenzoic acid.

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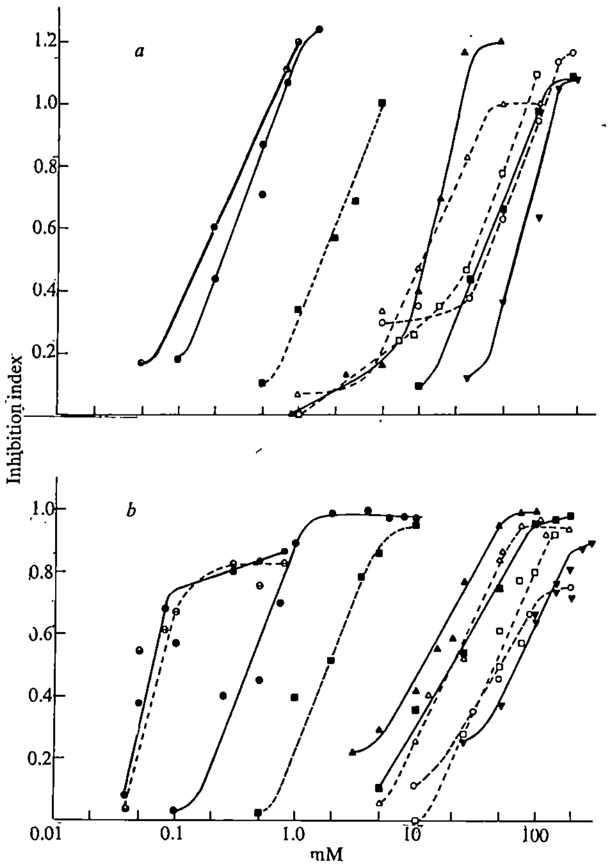

Fig. 1 Inhibition by fatty acids of *B. subtilis* growth and of serine uptake in membrane vesicles. Saturated fatty acids are identified by the number of carbon atoms (C_2=acetate, C_3=propionate, C_4=butyrate, C_6=hexanoate=caproate). *a*, Growth: *B. subtilis* (60015, requiring methionine and tryptophan) was shaken at 37° C in nutrient medium (buffered at *p*H 6.5 by 0.1 M phosphate)[4] to $A_{600}=0.5$. Aliquots were transferred to prewarmed Erlenmeyer flasks or large test tubes containing different amounts of the inhibitor (dissolved in water or ethanol). The same solvent was present in the control flasks. Using the difference ΔA between the A_{600} at 1 h and that at zero time for the experimental flasks and the corresponding value ΔA_c for the control flask, an inhibition index $= 1 - \frac{\Delta A}{\Delta A_c}$ was calculated. The short chain fatty acids (up to C_6) were used as potassium salts dissolved in water, at *p*H 6.5, while the long chain fatty acids were dissolved in ethanol and used in the buffered medium at low enough concentrations that the *p*H remained 6.5. The same extent of growth inhibition was observed with the prototroph *B. subtilis* strain (60009)[5] and also with *B. pumilis* (strains ATCC 4520, 4522, 6631) for acetate, propionate, butyrate, hexanoate, decanoate and sorbate. *b*, Serine uptake: membrane vesicles of *B. subtilis* (60015), grown in nutrient medium plus 10 mM glycerol (to induce glycerol-phosphate-dehydrogenase) to $A_{600}=1$, were prepared and tested (in 100 µl. final volume) for serine uptake in the presence of α-glycerol-phosphate as energy source, according to Konings and Freese[6]. The fatty acid (potassium salt in water or free acid in ethanol or dimethyl sulphoxide, final solvent concentration maximally 1%) was added to the reaction mixture containing the vesicles (1 mg ml.$^{-1}$ protein) and incubated at 25° C for 1 min before addition of glycerol-phosphate (20 mM) and ^{14}C-L-serine (15.6 µM). Three minutes after serine addition the reaction was stopped by 2 ml. 0.1 M LiCl (25° C) added to a 'Millipore' filter (pore size 0.45 µm) and washed twice with 2 ml. LiCl. The zero time values were obtained by adding the serine after the LiCl. Inhibition index $= 1 - \frac{\Delta U}{\Delta U_c} \approx \frac{U_c - U}{U_c - U_c^0}$ where U and U_c are uptake values after 3 min and U_c^0 is the uptake value of the control (or the fatty acid containing) sample at zero time. ⊖—⊖, Linoleate; ●—●, C_{10}; ■---■, C_8; ▲—▲, C_6; ■—■, C_4; ○---○, C_3; ▼—▼, C_2; △---△, sorbate; □---□, crotonate; ⊖---⊖, oleate.

uptake, however, does not necessarily prove that transport itself is inhibited; it may merely reflect the inhibition of metabolism, the unmetabolized compound preventing its own uptake. This objection is less valid for arsenate, whose metabolites are unstable, or for α-amino-isobutyric acid, which is not metabolized[8]. The objection can be generally ruled out by the use of membrane vesicles, which can be obtained from bacteria almost free of cytoplasmic components and whose transport depends strictly on the presence of an added energy source[6,8,11]. In membrane vesicles of *B. subtilis* the uptake of L-serine, energized by α-glycerol-phosphate or NADH, is inhibited by short and long chain saturated and unsaturated fatty acids (Fig. 1*b*), by parabens (Fig. 2*b*), and by other microbial growth inhibitors (Fig. 3*b*, and see Table 2). Because the inhibition index in this case cannot exceed 1, the concentration dependence of transport inhibition by different compounds is remarkably similar to that of growth inhibition. The only exception is sulphite, which has only a marginal effect on membrane transport. (Neither sulphite nor nitrite can serve as energy source.) Only high concentrations of

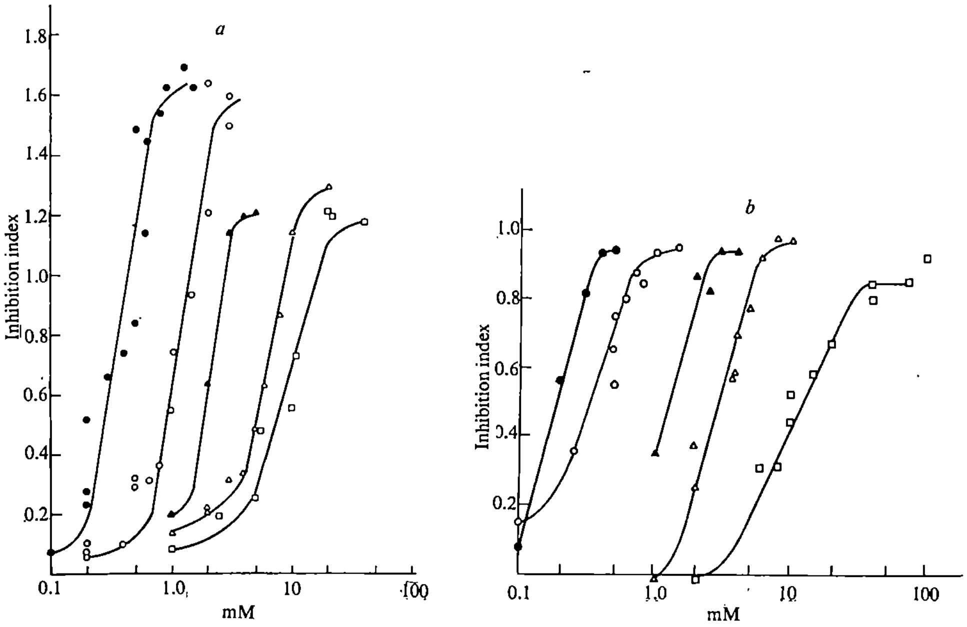

Fig. 2 Inhibition by parabens of (*a*) growth and of (*b*) serine uptake in vesicles. Conditions as in Fig. 1. Parabens were dissolved in ethanol. ●—●, Butyl; ○—○, propyl; ▲—▲, ethyl; △—△, methyl; □—□, *p*-hydroxybenzoate.

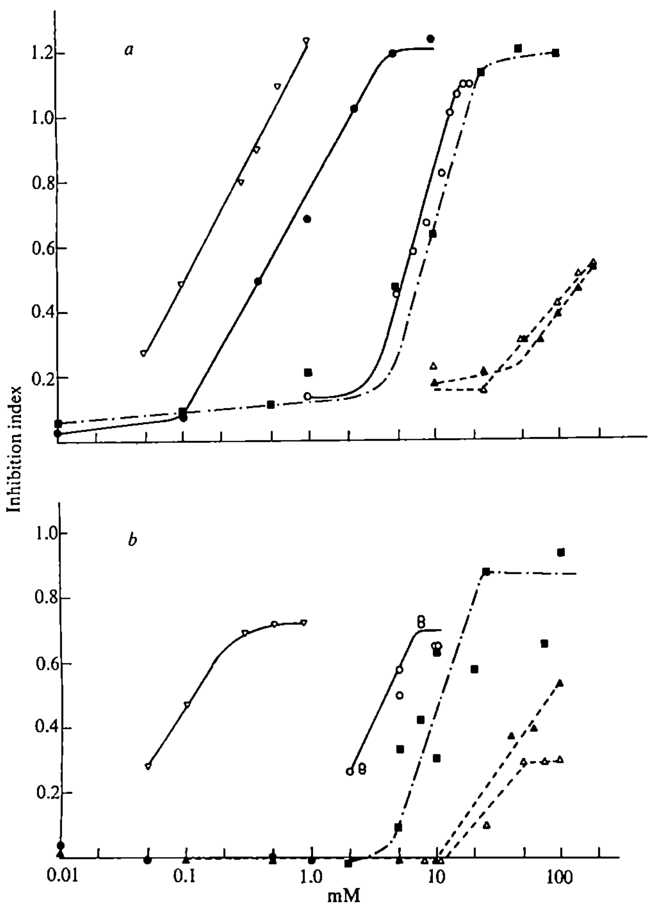

Fig. 3 Inhibition by miscellaneous compounds. *a*, Growth; *b*, serine uptake. Conditions as in Fig. 1. DNP, 2,4-dinitrophenol. The inhibition of growth by up to 50 mM nitrate was less than 3%. ▽—▽, DNP; ●—●, sulphite; ■—·—■, benzoate. ○—○, nitrite; △---△, ascorbate; ▲---▲, erythorbate;

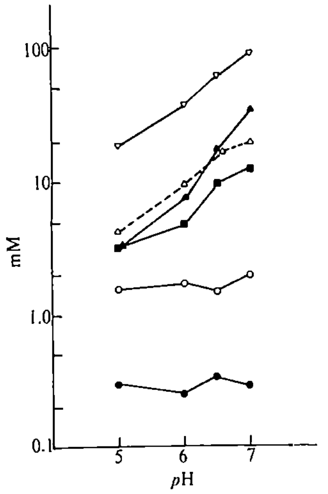

Fig. 4 *p*H dependence of 50% inhibitory concentration for serine uptake in membrane vesicles. Serine uptake was measured, as in Fig. 1*b*, at different *p*Hs and for different concentrations of inhibitors. The interpolated concentration values that would give 50% inhibition at a given *p*H are plotted for different *p*Hs. ▽—▽, C_3; ▲—▲, C_6; △---△, sorbate; ■—■, benzoate; ○—○, nitrite; ●—●, propyl paraben.

ascorbate or erythorbate inhibit membrane transport (these compounds do not energize transport).

The inhibition of active transport can be observed also for other amino-acids such as L-leucine, and for L-malate, whose uptake is also energized by glycerol-phosphate (Table 3). The interpolated concentration needed to inhibit vesicular serine transport by 50% is much lower at *p*H 5.5 than at *p*H 7 for propionate, hexanoate, sorbate or benzoate, but not for propyl paraben (Fig. 4), in agreement with the *p*K values. However, the inhibition by nitrite is not dependent on *p*H, indicating that vesicular transport is inhibited by the negatively charged nitrite ion. As we found, in agreement with published reports[2], that growth inhibition by nitrite increases with decreasing *p*H, some other reaction must contribute to the growth inhibition

Table 2 Inhibitory Effects of Different Compounds on Whole Cells and Membrane Vesicles of *B. subtilis*

		% Inhibition (=inhibition index × 100)						
				Membrane vesicles				
			Whole cells		Serine uptake		Oxidation	
Compound	Concentration	Growth	O_2	ATP	α-gly-P	NADH	α-gly-P	NADH
Alcohol	1%	12	0	0	0	10	0	0
Dimethyl sulphoxide	1%	0	ND	ND	0	0	0	0
Actinomycin D	10 μg ml.$^{-1}$	105	0	0	ND	ND	2	0
Chloramphenicol	100 μg ml.$^{-1}$	100	0	0	16	0	25	0
n-Decanoate	0.8 mM	107	85	78	88	72	1	0
Butyl paraben	0.5 mM	150	70	82	95	ND	37	62
Propyl paraben	1 mM	142	74	54	93	ND	26	50
Ethyl paraben	3 mM	80	74	49	95	ND	30	33
Methyl paraben	10 mM	115	62	54	95	ND	20	25
p-Hydroxybenzoate	20 mM	122	68	45	68	ND	46	0
Benzoate	20 mM	101	65	59	57	41	37	0
Sorbate	50 mM	101	80	61	85	61	47	0
Crotonate	80 mM	99	80	69	65	60	33	0
Nitrite	10 mM	66	86	58	78	ND	0	0
Acetate	200 mM	111	76	77	73	ND	0	0
Propionate	150 mM	114	83	68	67	71	0	0
Sulphite	10 mM	123	Aut.	84	0	ND	Aut.	Aut.
Ascorbate	200 mM	55	Aut.	3	44	ND	Aut.	Aut.
Erythorbate	200 mM	53	Aut.	10	80	ND	Aut.	Aut.

Aut. = Autoxidizes too rapidly.

For the inhibition in whole cells, *B. subtilis* strain 60015 was grown[4] to $A_{600}=0.5$, the cells were distributed to flasks containing the inhibitor, and the subsequent growth response was measured[5,8]. Without inhibitor the following values were found: exponential growth rate=1.4/h; oxygen consumption $(O_2)=293$ nmol (min $\times A_{600}$); ATP concentration (ATP)=2.9 nmol/A_{600}. Membrane vesicles were prepared from *B. subtilis* (60015) cells grown in nutrient medium[4] plus 10 mM glycerol (to induce glycerol-phosphate-dehydrogenase). Serine uptake was measured in membrane vesicles (1 mg/ml. protein) with 20 mM α-glycerol-phosphate (α-gly-P) or NADH as energy source as in Fig. 1. Oxidation of the substrates at the same concentrations was determined with 0.1 mg/ml. membrane protein. Without inhibitor the rates of serine uptake were with α-gly-P: 118 pmol/(min × mg protein) and with NADH: 62 pmol/(min × mg protein), while the rates of oxidation were for α-gly-P: 76 nmol/(min × mg protein) and with NADH: 186 nmol/(min × mg protein).

Table 3 Transport Inhibition of Leucine and Malate

Inhibitor	Concentration (mM)	% Inhibition of the uptake of Leucine	Malate
Propionate	150	85	64
Hexanoate	50	93	71
Linoleate	0.2	72	55
Propyl paraben	1.0	96	76

Uptake was measured as in Fig. 1. Without inhibitor the rates of uptake were for ^{14}C-(UL)-L-leucine (16 μM, 5 μCi ml.$^{-1}$); 28 pmol/(min × mg protein) and for ^{14}C-(UL)-K-malate (0.1 mM, 2.6 μCi ml.$^{-1}$): 208 pmol/(min × mg protein).

at lower *p*Hs. Part of it may be the lethal (and mutagenic) effect whose strength increases with decreasing *p*H[12].

Specificity of Inhibition

While *B. subtilis* is inhibited by all food preservatives, other microorganisms are inhibited only by some[2]. Growth inhibition of *Escherichia coli* by different saturated fatty acids, for example, is shown in Fig. 5*a*. About the same concentrations of short chain fatty acids, up to C_6, and DNP, inhibit the growth of *E. coli* as that of *B. subtilis*. But for C_8 about twice, and for C_{10} about fifty times the concentrations are needed, while no inhibition is observed with long chain fatty acids (Fig. 5*a*). The uptake of L-serine into *E. coli* cells is also not inhibited by concentrations of long chain fatty acids that completely inhibit growth or serine uptake in *B. subtilis* (Fig. 6). This lack of inhibition is not due to a particular property of the transporting membrane; in membrane vesicles of *E. coli* all fatty acids inhibit serine transport at the same concentrations as in vesicles of *B. subtilis* (Fig. 5*b*). The effective concentration of long chain fatty acids is apparently lower in the (transporting) membranes of whole *E. coli* cells than in the membranes of isolated vesicles. As a possible explanation for this difference, the long chain fatty acids that are partitioned into the membrane of *E. coli* might be so rapidly metabolized[13,14] that only much larger concentrations are inhibitory. *B. subtilis* cannot metabolize long or short chain fatty acids, and it can effectively use acetate only at high concentrations (50 mM)[15,16]. Alternatively, the lipopolysaccharide layer that typically surrounds the wall of Gram negative organisms could screen out the larger compounds. The latter explanation is the correct one, as will be reported elsewhere.

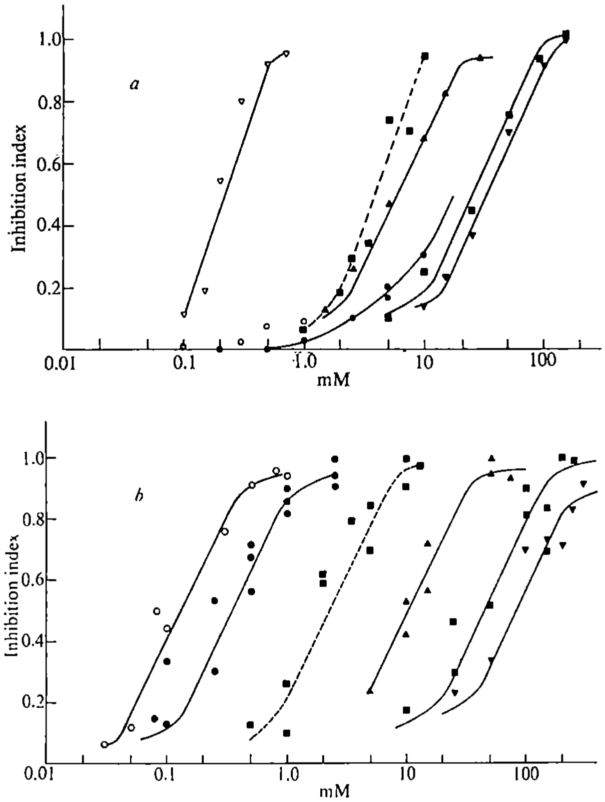

Fig. 5 Inhibition by different fatty acids of growth and serine uptake in membrane vesicles of *E. coli* (strain NF 161, which requires methionine and arginine). Growth inhibition (*a*) and vesicular transport (*b*) were measured as in Fig. 1. ▽—▽, DNP; ●—●, C_{10}; ■ - - - ■, C_8; ▲—▲, C_6; ■—■, C_4; ▼—▼, C_2; ○—○, linoleate.

In contrast to *B. subtilis*, concentrations of the fatty acids (up to C_8) which completely inhibit growth of *E. coli* do not reduce the concentration of ATP/A_{600} (measured after 20 or 40 min incubation). Apparently, some other compound is exhausted before ATP is used up.

Generalizations and Future Studies

Lipophilic acids, including preservatives, somehow uncouple[8,17] both substrate transport and oxidative phosphorylation from the electron transport system. They apparently inhibit growth principally by inhibiting the cellular uptake of amino-acids, organic acids, phosphate and so on, because in whole cells these two inhibitory phenomena are strictly correlated, whereas the concentration of ATP does not necessarily decrease (in the facultative anaerobe *E. coli*). In contrast to saturated fatty acids and DNP, which only uncouple[8], unsaturated fatty acids and parabens partially inhibit also the electron transport system itself (Table 2). Exceptional preservatives are sulphite, which does not inhibit transport, and nitrite, for which the inhibition of growth but not of transport increases with decreasing *p*H.

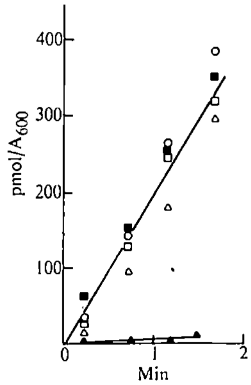

Fig. 6 Serine uptake of resting cells of *E. coli*. *E. coli* cells were grown to $A_{600}=0.28$, washed twice on 'Millipore' filters, resuspended in N medium[4], and starved for 90 min at 25° C. The rate of ^{14}C-(U)-L-serine (0.62 μM, 0.08 μCi ml.$^{-1}$) uptake was measured[8]. ○, No addition; ■, 5 mM linoleate; □, 0.5 mM linoleate; △, 2 mM C_{10}; ▲, 20 mM C_{10}.

Some organisms are resistant to certain lipophilic acids. If the transport comparisons of *E. coli* membrane vesicles and whole cells can be generalized, the resistant organisms seem to prevent the accumulation of the inhibitor on the transporting cell membrane. In any case, the resistance of some (Gram negative) organisms to long chain fatty acids can be used to select for them among sensitive (Gram positive) organisms.

Because membranes of all organisms contain phospholipid bilayers, some antimicrobial lipophilic acids must also inhibit human cells; inhibitors with low *p*K should be particularly effective in the highly acidic intestinal fluid. A comparison of the inhibition of growth, transport, or nerve function of human cells with that of microorganisms should reveal which preservatives are least harmful to man. For example, it may be possible to replace nitrites and sulphites, which induce mutations[12,18] and of which nitrite can produce carcinogenic nitrosamines[19], by other inhibitors and colour fixatives which do not involve the potential hazard of genetic damage on somatic or germ cells.

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Boundary between Continental and Oceanic Crust at the Margin of Rifted Continents

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From a detailed study of the continental margin off Norway we have been able to establish the presence of two buried marginal escarpments—Vøring Plateau Escarpment and the Faeroe Shetland Escarpment. We believe that these escarpments together with a segment of the Jan Mayen Fracture Zone between them define quite clearly the boundary between the continental and oceanic basement. We describe these findings and discuss their application to other continental margins.

Two buried marginal escarpments off Norway—Vøring Plateau and Faeroe Shetland (Fig. 1)—define the landward boundary of buried basement highs on the continental slope[1]. The basement highs are a direct continuation of the typical oceanic basement which lies seaward. Landward of the basement highs there is a large marginal sedimentary basin in which the maximum sediment thickness exceeds 7 km.

Continental Margin off Norway

Fig. 2 shows a structure section across the Vøring Plateau Escarpment based on velocities obtained from seismic refraction and wide angle reflexion data. We also show four projected isostatic gravity and residual total intensity magnetic profiles. The sedimentary section northwest of the Vøring Plateau Escarpment is less than 2 km thick and the seismic velocity of the layer overlying basement is about 2.2 km s^{-1}. The oldest identifiable magnetic anomaly northwest of the escarpment is believed to be anomaly 24 (60 m.y. BP, ref. 2) and thus the basement is early Tertiary in age. Southeast of the escarpment there is a large increase in sediment thickness. The seismic velocities in the lower part of the sedimentary sequences are significantly higher than those above Tertiary basement northwest of the escarpment. Although the seismic velocities would be expected to increase with increased thickness of Tertiary sediments, in the adjacent North Sea basin the Tertiary sedimentary section has a velocity almost always less than 2.5 km s^{-1} even where it is a few km thick. Velocities higher than 2.5 km s^{-1} in the North Sea have been associated with sediments of Mesozoic and Late Palaeozoic age. We believe that there is a similar velocity-age relationship for the sediments on the Norwegian Shelf. Support for this belief comes from the known occurrence of Mesozoic outcrops on the shelf. The shelf sediments thicken progressively seawards with maximum thickness on the slope. We infer that the marginal sedimentary basin is a continuation of the North Sea basin and has, in addition to the Cainozoic sediments, a thick Mesozoic sequence and probably also a sequence of Late Palaeozoic sediments. Thus there is a significant contrast in age of the basement across the escarpments and most of the sediments in the basin predate the Early Tertiary opening of the Norwegian Sea.

In Fig. 2 we show the pronounced change in magnetic

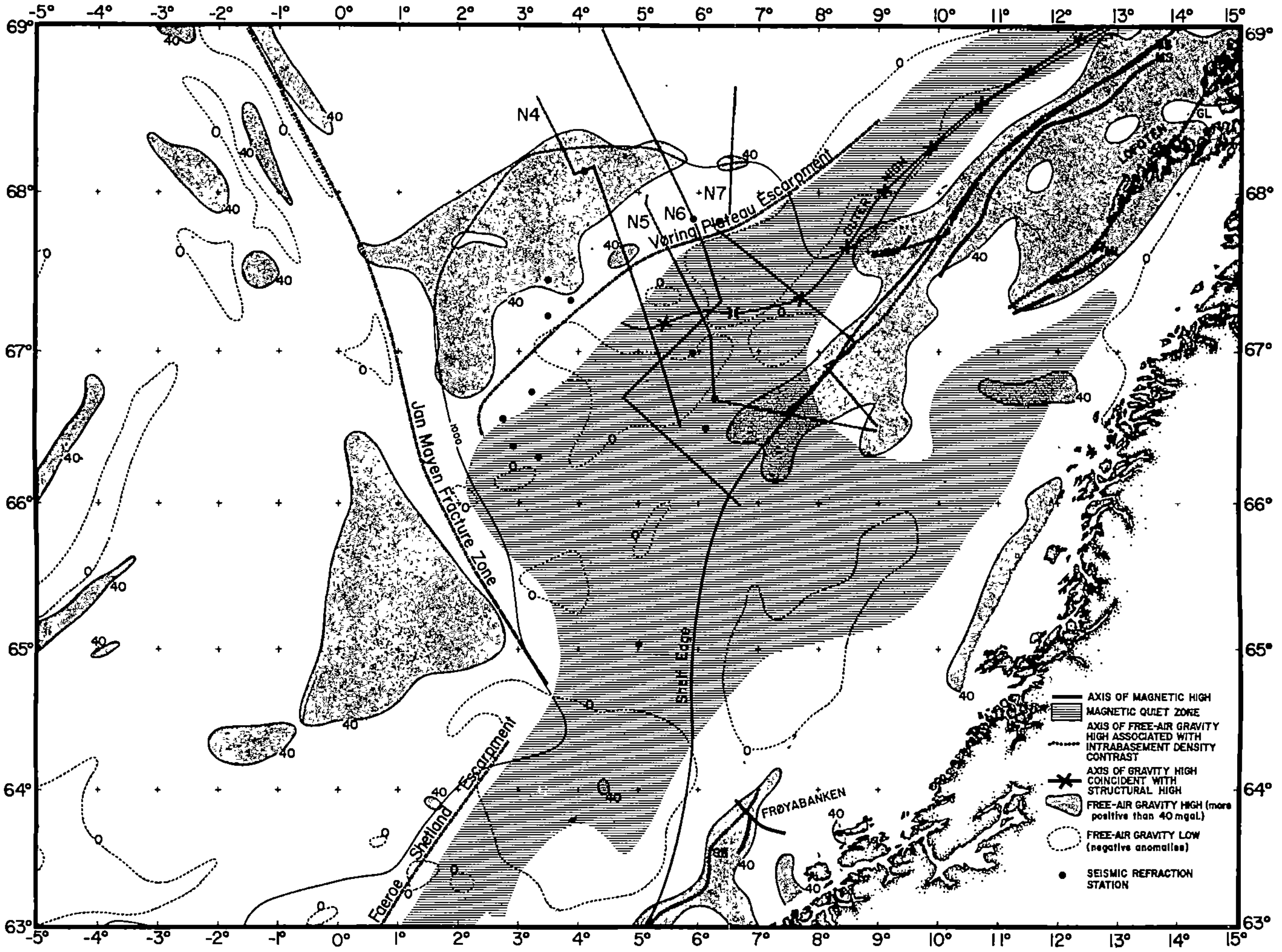
-5° -4° -3° -2° -1° 0° 1° 2° 3° 4° 5° 6° 7° 8° 9° 10° 11° 12° 13° 14° 15°
69° 68° 67° 66° 65° 64° 63°
N4
N5
N6
+N7
Vøring Plateau Escarpment
Outer High
MS
GS
ML
GL
LOFOTEN
Jan Mayen Fracture Zone
Shelf Edge
Faeroe–Shetland Escarpment
FRØYABANKEN
1000
40
0
AXIS OF MAGNETIC HIGH
MAGNETIC QUIET ZONE
AXIS OF FREE-AIR GRAVITY HIGH ASSOCIATED WITH INTRABASEMENT DENSITY CONTRAST
AXIS OF GRAVITY HIGH COINCIDENT WITH STRUCTURAL HIGH
FREE-AIR GRAVITY HIGH (more positive than 40 mgal.)
FREE-AIR GRAVITY LOW (negative anomalies)
SEISMIC REFRACTION STATION

Fig. 1 Prominent gravity and magnetic features of the Norwegian continental margin. We believe that the gravity and magnetic lineations on the shelf are caused primarily by intrabasement density and magnetization contrast, although a small amount of basement relief (~1 to 2 km) also seems to be associated with belts of Pre-Cambrian age. The gravity "Outer High" is believed to be a structural high. Note that gravity lows exist between the shelf edge and the escarpment. The magnetic quiet zone crosses the shelf edge between 64 and 66° N. The 1,000 fm contour is indicated.

anomalies at the escarpment. Seaward the anomalies form linear patterns characteristic of seafloor spreading. Landward the magnetic anomalies are very subdued and constitute a magnetic quiet zone. Between 65° N and 67° N the magnetic quiet zone extends across the shelf edge (Fig. 1). It has been argued that the magnetic quiet zones over deep sedimentary basins can be attributed to increased depth to magnetic basement or to thermal effects of a large thickness of sediment which in some way alters the magnetic properties of the underlying basement rocks. But by upward continuation we can show that the higher amplitude magnetic anomalies observed seaward of the Vøring Plateau Escarpment are not explained simply by a smaller depth to basement. We also note that over the Outer High (Fig. 1), which has been interpreted as a structural high[1] and where basement (from reflexion profiler data) is known to be buried under less than 2 km of sediments in some areas, there are no large magnetic anomalies (Fig. 2). But large magnetic anomalies exist over some portions of the continental shelf where basement is buried under several kilometres of sediment. Adam[3] shows several examples of such anomalies where depths of up to 8 km to basement are estimated. The magnetic anomaly at Frøyabanken (63° 50′ N, 7° E) is especially prominent. The anomaly exceeds 1,300 gamma. Depth to basement has been estimated to be about 4 km.

Therefore, we believe that the magnetic quiet zone over the Norwegian continental margin cannot be attributed to a large thickness of sediments. Rather, the basement rocks possess different magnetic properties. We suggest that continental basement lies landward of the escarpment and oceanic basement lies seaward.

A major change in basement elevation should be expected at the boundary between oceanic and continental crusts. The density of the continental crust must be different from that of the newly formed oceanic crust and, unless densities in the underlying mantle are rearranged in a peculiarly coincidental way, isostasy requires the two kinds of crusts to be balanced with different resultant elevations. Differences in basement elevation are observed for both the Vøring Plateau Escarpment and the Faeroe–Shetland Escarpment but are not reflected in topography due to the deposition of a large thickness of Cainozoic sediments. The steep gradient in the isostatic anomaly profiles at the escarpment (Fig. 2), however, is also indicative of change in basement elevation.

Prominent magnetic and gravity anomaly belts exist on the shelf off Norway (Fig. 1). MS and GS lie at the shelf edge; ML and GL which seem to be similar in nature exist over the Lofoten Islands. Two lines of argument suggest that the rocks giving rise to these anomalies are very old. First, these belts seem to be associated with Pre-Cambrian rocks in the Lofoten Islands as well as at the Laxfordian and Scourian assemblages of northwest Scotland which are also of Pre-Cambrian age. We have been able to show that belt GS runs into Scotland. Second, the magnetic maximum MS is systematically landward of the gravity maximum GS. If both the gravity and magnetic anomalies are attributed to the same body the angle of inclination of magnetization must be very small[1]. Large values of Q would then imply that the direction of remanent magnetization has a small inclination; smaller values of Q would imply a still smaller inclination or a reversed direction of remanent magnetization. These observations do not exclude a Pre-Cambrian age for these belts.

Perhaps the most important question raised by the great age of these belts is the circumstance of their location at the shelf edge. There has been considerable speculation as to the origin of gravity and magnetic highs near the edge of continental shelves, which seem to be associated in general with rocks of different ages[5]. In our view, the gravity and magnetic highs on the Norwegian shelf do not occur as a result of a location near the shelf edge, but rather the location of the shelf edge is predetermined by high density belts extending deep into the crust. The distribution of sediments deposited prior to the opening of the Norwegian Sea indicates that the thickness over these belts has been relatively the smallest. We infer that these belts underwent the least pre-opening subsidence. After the opening these belts have been similarly resistant to subsidence and appear to define a hinge line for the post-opening subsidence of the area between the shelf and the marginal escarpments.

Continental Margin off South Africa

We have also investigated the continental margin off South Africa (Fig. 3). A magnetic quiet zone exists over the shelf and the upper slope. On the southeast side the magnetic quiet zone is bounded by a prominent linear anomaly situated near the base of the slope[6] (Fig. 4). This magnetic anomaly is associated with a fracture zone (J. Frencheteau and X. LePichon, unpublished), here named the Agulhas Fracture Zone. In Fig. 6 the topographic, gravity (isostatic) and magnetic profiles are shown for the V1810 crossing. We note that the magnetic profile shows no change in character at the shelf edge but near the base of the slope a large anomaly coincides with a large gradient in the isostatic gravity profile. Seaward of this point the magnetic field is much more irregular. Other magnetic profiles which cross the fracture zone from the shelf to the deep sea show similar characteristics. On the other hand, the magnetic profiles crossing the fracture zone where there is deep ocean on either side do not exhibit any noticeable change in pattern (Fig. 4).

Seismic reflexion profiler records (Fig. 3) show that oceanic basement can be followed westward from the basin to the base of the slope. Basement is not seen landwards of the fracture zone. We attribute this to a greatly increased thickness of sediment. Many seismic refraction results have been obtained in the area[7–10]; in Fig. 3 we show three typical profiles. Seaward of the Agulhas Fracture Zone the M discontinuity is found at depths associated with a typical oceanic structure. Landward of the fracture zone depths to M have not been obtained. But for continental shelves generally and this shelf particularly (because of the continuity of land structures beneath the shelf[8–10]) the crust is considered to be continental in nature. The area in which the nature of the crust is in question seems to have been the area between the shelf edge and the fracture zone. But we believe that the absence of any difference in the character of the magnetic anomaly at the shelf edge demonstrates clearly that the boundary between oceanic and continental basement is near the base of the slope rather than at the shelf edge.

Profiles across the continental margin west of Cape Town are shown in Fig. 5. A steep gradient in the isostatic gravity profile is associated with the initial appearance of the sea-floor spreading type magnetic anomalies. The relative positions of the gravity and magnetic anomalies with respect to the topography are seen best in profile C1314a in Fig. 6. The magnetic high M (Figs. 3 and 5) on the slope has been followed northwest to 31° N (ref. 12).

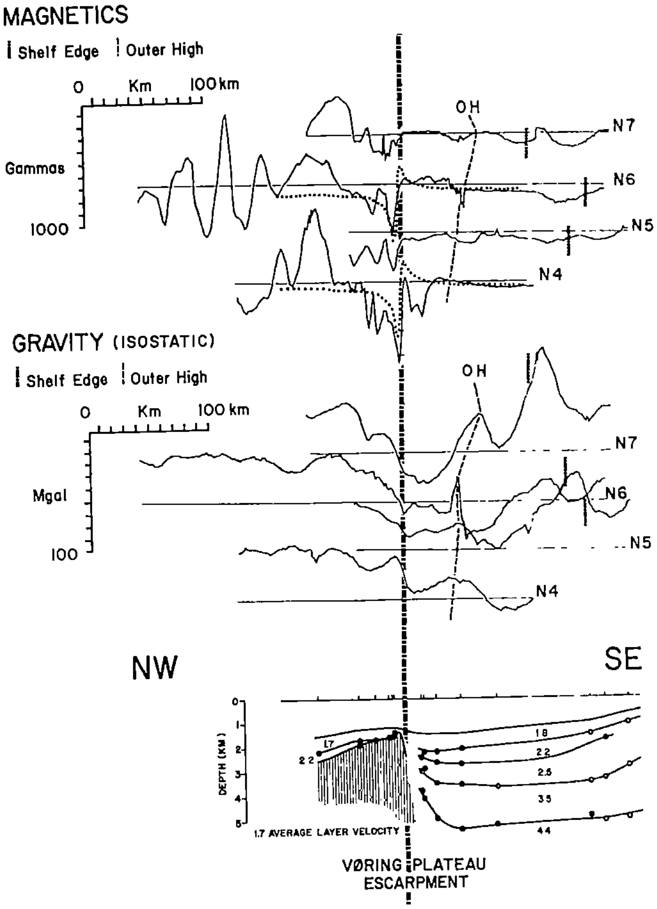

Fig. 2 Profiles of magnetic and isostatic gravity anomalies and a seismic structure section across the Vøring Plateau Escarpment. The location of profiles N4–N7 shown in Fig. 1. The profiles are projected normal to the escarpment. The subdued nature of the magnetic anomalies southeast of the escarpment is quite apparent. In profile N4 the escarpment is not as steep as in other profiles and the magnetic anomaly landward of the escarpment is associated with basement topography. The computed anomaly caused by a semi-infinite horizontal plate 0.5 km thick lying seawards of the escarpment and with its edge coincident with the escarpment is superimposed on magnetic profiles N6 and N4. The top of the plate is at a depth of 1.5 km and it is assumed to be magnetized with an intensity of magnetization 0.012 e.m.u. in a direction opposite to the direction of the present dipole field (which is very close to the direction of the Earth's gravity field in the Early Tertiary). The line OH (also see Fig. 1) which delineates a structural high is determined from the isostatic gravity anomaly and seismic reflexion profiler data. The seismic section is constructed by projecting station positions on a profile normal to the escarpment. The station positions are shown in Fig. 1. Black dots indicate layer boundaries. Average layer velocities are shown. Note that no stations are located on the Outer High which is therefore not reflected in the seismic section.

Comparison of the Two Margins

Comparing the Norwegian margin to the South African margin, the Agulhas Fracture Zone corresponds to the Jan Mayen Fracture Zone, and the seaward edge of the magnetic quiet zone west of Cape Town appears to correspond to the marginal escarpment off Norway.

We have made model calculations to match the magnetic anomalies at the Vøring Plateau Escarpment, the marginal

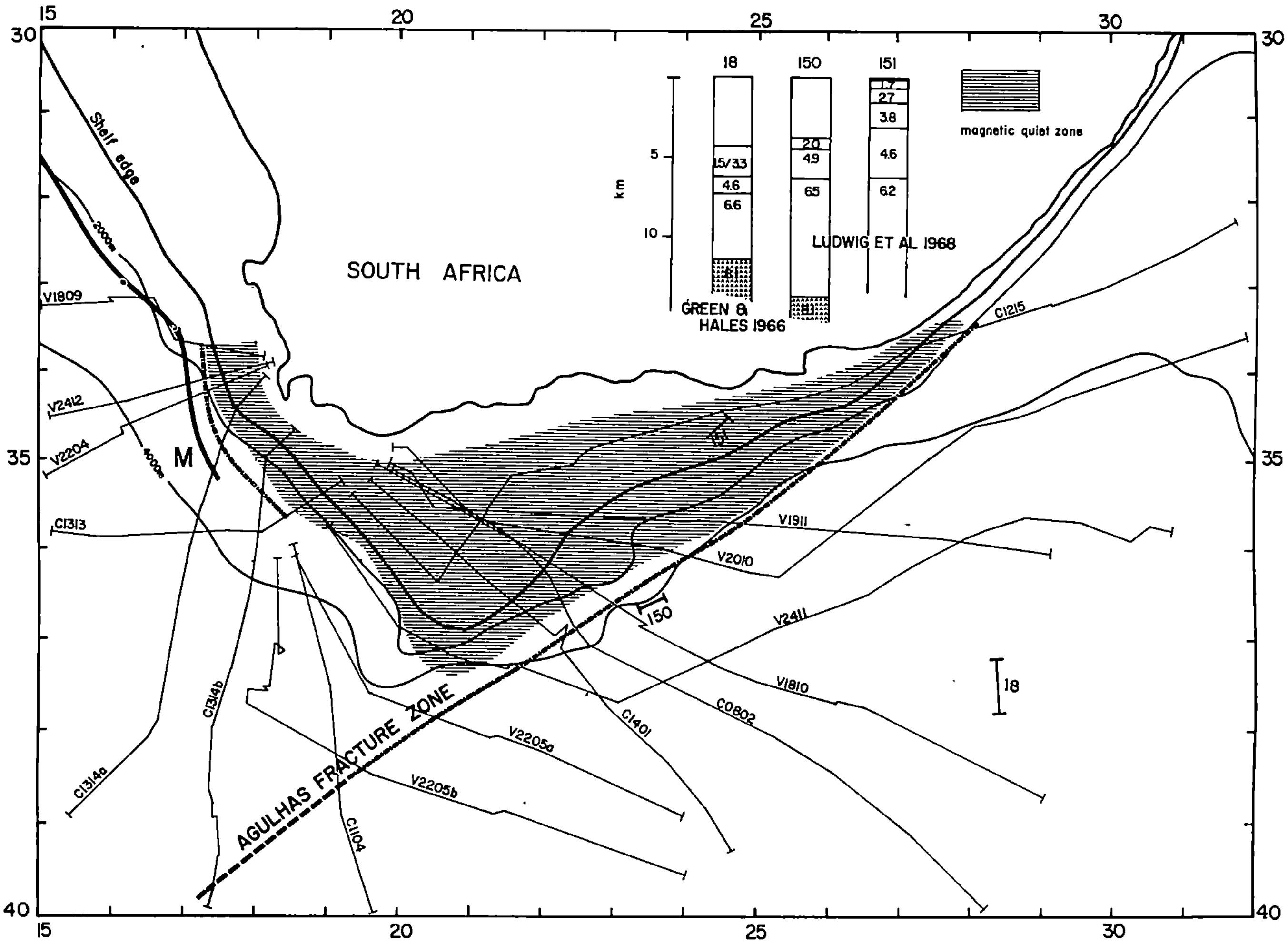

Fig. 3 Prominent gravity and magnetic features of the South African continental margin. The Agulhas Fracture Zone near the base of the continental slope is coincident with a steep gradient in the isostatic gravity anomaly and a peak in the magnetic total intensity anomaly. A similar line on the western margin on the continental slope is also associated with a steep gradient in the isostatic gravity anomaly. A peak in an associated magnetic anomaly, M, lies some distance seaward and is continued further north from the data of Simpson and duPlessis[11]. Seismic refraction profile 151 (ref. 8) is typical of a number of profiles located on the shelf; profiles 150 and 18 (refs. 7, 8) are representative of oceanic crustal structure.

anomalies west of Cape Town and at the Agulhas Fracture Zone.

Northwest of the Vøring Plateau Escarpment the seafloor spreading type basement is associated with reversely and normally magnetized stripes parallel to the escarpment. We have calculated the anomaly corresponding to the edge of a reversely magnetized plate (Fig. 2). The prominent negative anomaly at the escarpment is reproduced by this model. Westward the observed anomalies fluctuate about the level of the model anomaly, which is not unexpected because we did not consider the changes of polarity in the adjacent stripes. A similar calculation for the edge of a normally magnetized plate is made to match the slope anomaly west of Cape Town (Fig. 6). If our models are correct, we deduce that the opening of the Norwegian Sea took place in a period of reversed polarity while the South Atlantic opened in a period of normal polarity. Off the Agulhas Fracture Zone the magnetic stripes are presumably perpendicular to the fracture zone; but we believe that the fracture zone is characterized by a zone of ultramafic rocks for which the magnetization is primarily induced, and we have computed the anomaly caused by the edge of a plate magnetized by induction in the Earth's present field. The fit of the model to the observed anomaly is quite good (Fig. 6).

We have observed a large gradient in the isostatic gravity anomalies at the suggested boundary between continental and oceanic basement. In part, at least, this gradient reflects the thicker section of sediments on the landward side of the boundary. In any event, the gravity low between this boundary and the shelf edge appears to be diagnostic of the subsided continental crust and could be of great use in examining other continental margins. We have used isostatic anomalies rather than free air anomalies. Free air anomalies at continental margins exhibit "edge effects" which arise from the difference in the gravitational effects of topography and its compensation. These edge effects tend to mask anomalies caused by local density inhomogeneities which are much better revealed by isostatic anomalies. Of course, isostatic anomalies are subject to error because of lack of knowledge of the completeness and mode of compensation. For stable margins, however, even a considerable variation in isostatic model causes only minor changes in the isostatic anomalies and therefore even though the model may be wrong in detail the isostatic anomalies provide very useful information. Both on the western and the southeastern margin off South Africa free-air highs on the shelf edge are considerably reduced and the anomalies on the slope are enhanced when the isostatic reduction is made.

There is considerable uncertainty as to the detailed crustal structure of most continental slopes. The area of the slope is generally quite close to isostatic equilibrium but seismic refraction stations[12] do not reveal the simple Airy com-

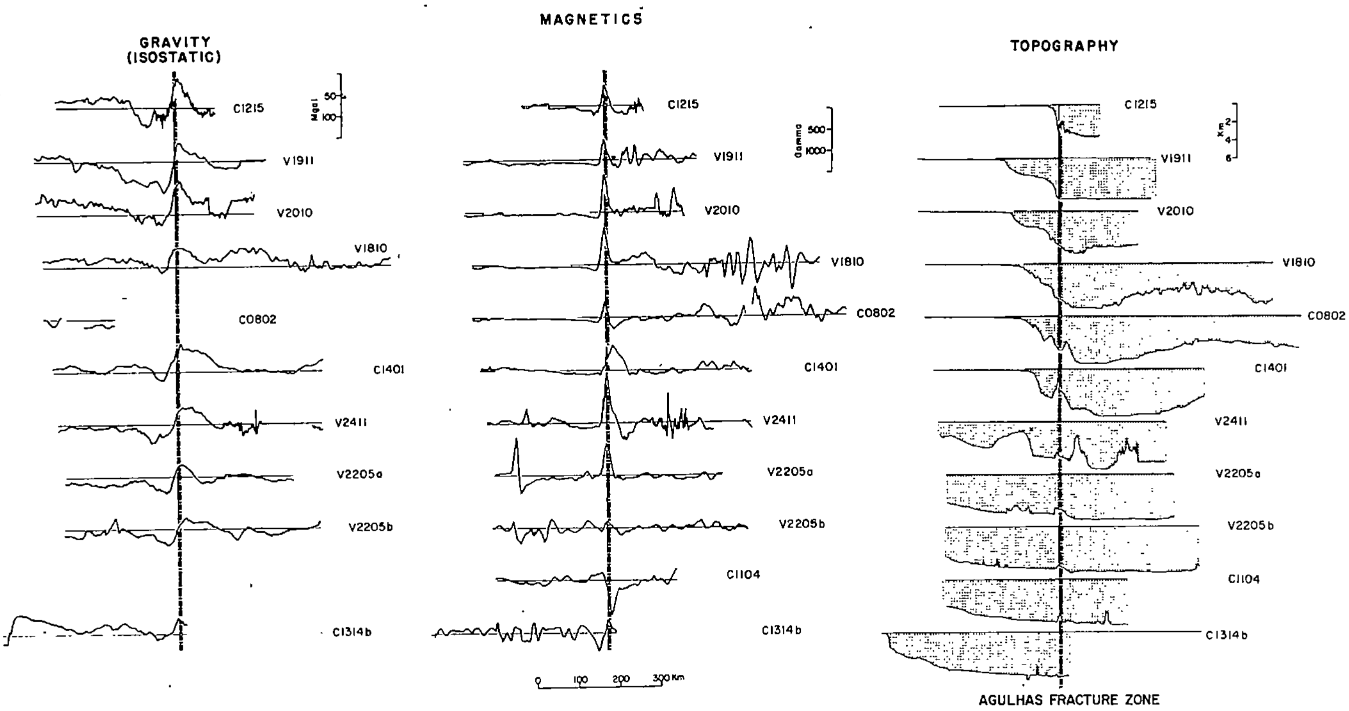

Fig. 4 Projected profiles of isostatic gravity anomalies, magnetic anomalies and topography across the Agulhas Fracture Zone (for locations see Fig. 3). North of profile V2411 the Agulhas Fracture Zone lies between the shelf and the deep ocean; south of profile V2205a it has deep ocean on either side. There is a steep gradient in the isostatic gravity anomaly associated with the fracture zone. This gradient is especially prominent in the northern profiles, as is a large magnetic positive anomaly.

pensation scheme implied by a smooth change in depth to the mantle from ocean to continent on most stable continental margins. As a general rule the velocities for both layer 3 and the mantle are lower under the slope and show much more variability than they do under the normal ocean. If the continental slope indeed represents subsided continental crust, an exact determination of the seismic structure would give an indication on how isostatic compensation is achieved for subsided margins. A comparison of seismic velocities between subsided and unsubsided areas could also give important information as to the nature of rocks comprising the crust.

The boundary discussed above has obvious implications for the reconstruction of rifted continents in that it represents the line of initial rifting. We do not, however, intend to imply that there has been no deformation in what we have called the subsided continental zone. It is unlikely that the continents rifted with a clean break at this boundary. Rather, as widely suggested, the extrusion of oceanic crust was probably preceded by a period of stretching and thinning of the continental crust achieved in part by normal faulting. Therefore, in the subsided zone it is perhaps more correct to speak of a continental basement over a modified crust rather than to imagine an undeformed continental crust. Strictly speaking, a complete reconstruction would not be made just to this boundary, but would

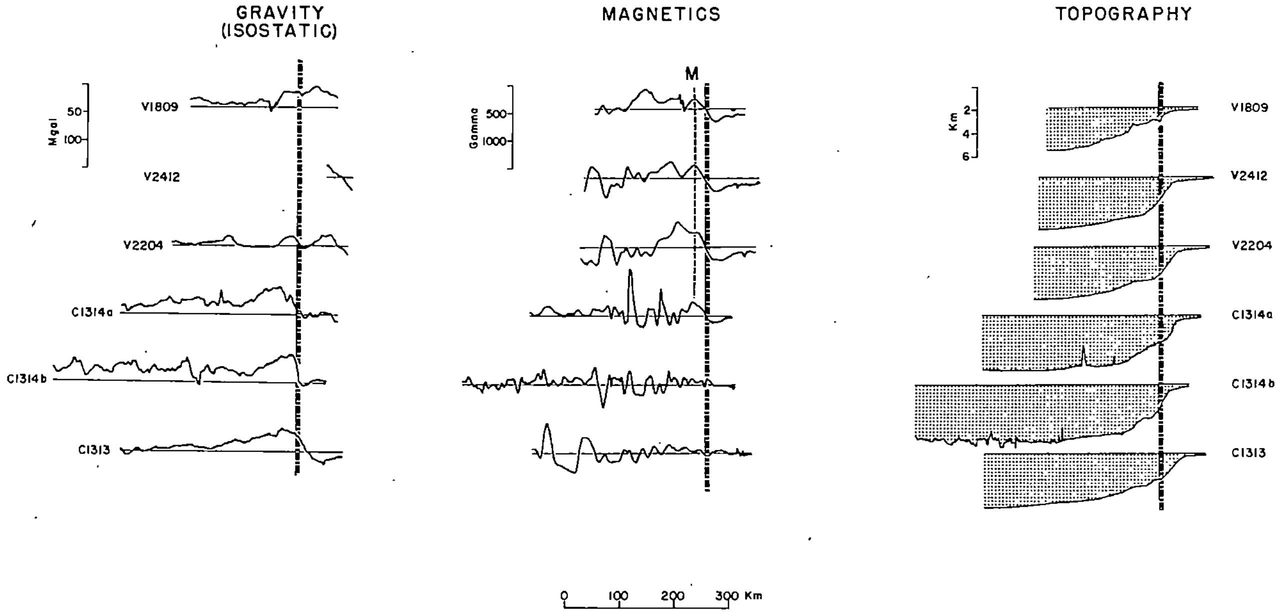

Fig. 5 Projected profiles of isostatic gravity anomalies, magnetic anomalies and topography across the western margin off South Africa. The reference line marks a steep gradient of the isostatic gravity anomalies. The magnetic maximum M lies further west.

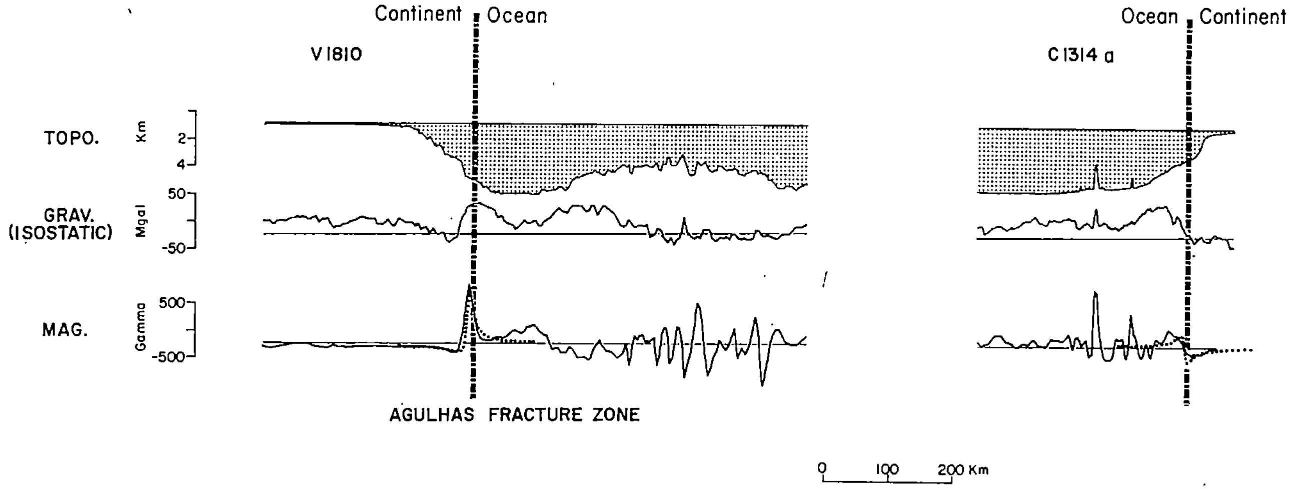

Fig. 6 Left: topography, isostatic gravity and magnetic anomaly profiles V1810. Note that the shelf break is not reflected in the magnetic anomaly and that isostatic gravity profile has a low in the area between the shelf break and the Agulhas Fracture Zone. The dotted curve is the computed anomaly caused by a semi-infinite horizontal plate 2 km thick lying seaward of the fracture zone and with its edge coincident with the fracture zone. The top of the plate is at a depth of 4 km and it is assumed to be magnetized by induction with a susceptibility of 0.04 cgs units. Right: topography, isostatic gravity and magnetic anomaly profiles C1314a. The dotted curve is the computed anomaly caused by a semi-infinite horizontal plate 1 km thick lying seaward of the reference line in Fig. 5. The top part of the plate is at a depth of 4 km magnetized in a field with declination 322.5° and inclination $-62°$. These are directions of the Earth's magnetic field in the Late Jurassic in South Africa[4]. Intensity of magnetization is 0.012 e.m.u.

in addition have to allow for the stretching of the continental crust.

Other Margins

In applying our thesis to other areas two qualifications are necessary. The first derives from the nature of continental basement, which is not always characterized by a lack of magnetic anomalies. Second, some magnetic quiet zones in oceanic areas are attributed to a lack of magnetic reversals[10,14–16]. The seaward portion of the magnetic quiet zone in the western North Atlantic has been attributed to an interval of constant magnetic polarity[13,16,17]. This does not rule out the possibility that the inner (landward) portion of the western North Atlantic quiet zone is also a marginal quiet zone of the type discussed here. In fact, within the western North Atlantic quiet zone a prominent magnetic lineation called the Blake-Spur anomaly[14,18] trends northeastwards from 30° N, 76° W. The magnetic pattern is considerably more subdued in the area landward of this anomaly (which may represent subsided continental crust) than seaward which represents an oceanic quiet zone due to an interval of constant magnetic polarity in the Jurassic[17].

A prominent escarpment near the base of the slope exists off the coast of West Africa between 13° S and 5° S (ref. 19) which possibly marks the boundary of continental and oceanic crust. Further north Arens *et al.*[20] have mapped the "continental rise fault" between the St Paul and Romanche fracture zones in the Gulf of Guinea. The basement is several km deeper on the landward side of this fault. The "continental rise fault" may mark the boundary of continental and oceanic basements. The possibility also exists that the deep sedimentary basin lying between Fuertaventura in the Canaries and Africa[21] is also underlain by continental basement. We consider this possibility because the oldest sediments in this basin are believed to be Upper Palaeozoic (and therefore deposited before the initiation of the North Atlantic opening) and because the area is magnetically quiet except for the presence of a single anomaly which trends obliquely across the bathymetry on to the shelf. It is of some interest to speculate that the marginal magnetic quiet zones south of Australia and north of Antarctica[23] also represent subsided continental crust.

We feel that it is important to establish the presence of the boundary between oceanic and continental basements at various rifted continental margins. As outlined here, this boundary is characterized by a contrast in depth and age of basement and the nature of magnetic anomalies on either side as well as by the presence of negative isostatic anomalies on the landward side.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Record-breaking Cosmic Ray Storm stemming from Solar Activity in August 1972

AN unusual centre of solar activity was the seat of the most severe disturbances of the current solar cycle early in August 1972. It produced reports from the general public of various visual phenomena in the night sky, surges in electrical systems, radio blackouts and effects upon the navigation of birds in flight. Of the great variety of physical phenomena associated with this remarkable region (sunspot group 331, McMath plage region 11976, centred at Carrington, longitude 009 degrees), we will concentrate on a description of the gross features of the greatest cosmic ray storm ever observed that commenced on August 4, and of which sunspot group 331 was the ultimate source.

A cosmic ray storm comprises a superposition of Forbush decreases, that is, a series of sudden reductions in the intensity of the galactic cosmic radiation[1]. Although cosmic rays have been recorded continuously with ground-based detectors for almost four decades[1], only one event of comparable magnitude had been observed previously. That was in July 1959, during the epoch when solar activity was greater than at any time since Galileo first observed sunspots in 1610 (ref. 2). In that case, the nucleonic intensity at a polar station was reduced to 24% below the pre-storm level seven days and three Forbush decreases after onset[1]. But the cosmic ray storm of August 1972 occurred near the minimum of an unspectacular solar cycle, and the magnitude of the decrease reached 27% in about twenty-four hours.

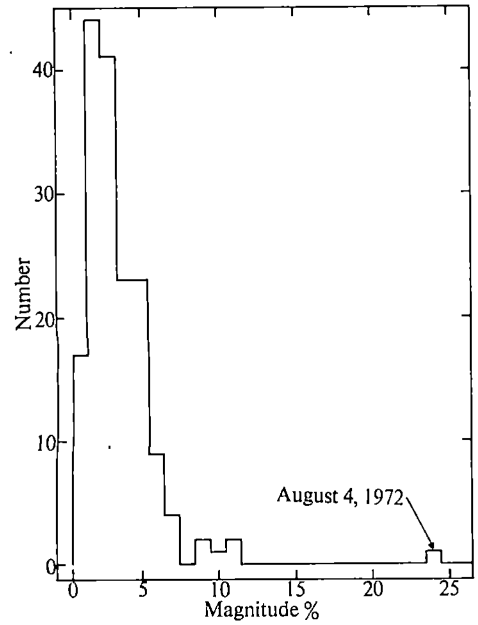

Fig. 1 Histogram showing the size distribution of transient nucleonic intensity reductions, as observed at a station with directions of viewing near the equatorial plane, and for which the lower energy threshold is close to the atmospheric cutoff. All significant cosmic ray storms or individual Forbush decreases that occurred during an eleven-year period (July 1961–August 1972) corresponding to the duration of a complete sunspot cycle are included. As the frequency of occurrence and average magnitude is greater near solar maximum[8], the storm commencing on August 4, 1972, during the waning portion of the current solar cycle, is clearly anomalous.

The unusual character of this event is further revealed in Fig. 1, which shows the distribution in the size of cosmic ray storms as observed with a detector viewing the equatorial plane to minimize the effects of north–south anisotropies in the modulation. From July 1961 to August 1972, corresponding to the period of one solar cycle, more than 90% of the intensity decreases were $\leq 6\%$, and the maximum flux reduction was only half as great at it was in the present case.

Region 331 was born on the visible disk of the Sun near N 13° W 36° on July 11, 1972. Its first passage, terminating on the west limb on July 15, did not presage the great burst of activity that followed its return to the east limb on July 29. The maximum area of the spot group, about 1,200 millionths of the hemisphere, and extending over about 17 degrees in longitude, was attained on August 4. The region appeared as a single large penumbra containing an intense magnetically complex umbral structure and several distinguishing characteristics.

The cosmic ray storm that commenced at 0130 UT on August 4 is shown in Fig. 2, which is a plot of the time variation of nucleonic intensity as recorded at a mid-latitude station for which the asymptotic directions of viewing lie near the equatorial plane, and the geomagnetic threshold rigidity (1.9 GV) is close to the atmospheric cutoff. It followed three large solar flares that were observed optically (H_α) to commence on August 2 at 0316 UT (Importance 1B, N 14° E 35°), 1838 UT (1B, N 13° E 28°) and 2005 UT (2B, N 13° E 28°). These flares produced the most severe disturbances during the current solar cycle in the many diverse phenomena that are included within the domain of solar-terrestrial physics.

The ledge that appears in Fig. 1 during the onset stage of the initial Forbush decrease FD-1 will be discussed later in the light of observations at other stations in the Bartol neutron monitor network. It terminated at about 2130 UT, when the intensity dropped abruptly to the minimum FD-2, at a rate exceeding 5% per hour during some intervals. While the galactic cosmic ray flux was recovering, an Importance 3B flare that started at 1500 UT (N 14° W 38°) on August 7 produced a ground level event (GLE) representing the arrival of relativistic solar protons beginning at about 1530 UT. This apparently "typical" GLE was followed by a small Forbush decrease FD-3, after which the galactic intensity gradually returned to the predecrease storm level.

Data recorded at polar stations for which the symptotic directions of viewing lie outside the equatorial plane[3] not only provide further insight into the characteristics of this cosmic ray storm, but are also relevant in interpretations of the observations of the majority of stations in the world-wide neutron monitor network which are located at lower latitudes[4]. Fig. 3 shows the intensity profiles at Thule (Greenland) and McMurdo and South Pole (Antarctica).

An anisotropy in the direction perpendicular to the ecliptic plane is a characteristic feature of cosmic ray storms[5], and produces a north–south asymmetry which manifests itself in systematic differences in the magnitude of a Forbush decrease and/or in the onset times in the two polar regions. A precise determination of the time of commencement of FD-1 in Fig. 3 reveals that it occurred about 2 h earlier at Thule. Presumably as a consequence of this delay, the magnitude of FD-1 at Thule was larger during the first six hours. On the other hand, although the onset of FD-2 at the northern station also preceded the start of this phase of the storm in Antarctica, the extent of the decrease at McMurdo was greater for several hours. At 0130 UT on August 5 the magnitudes of the intensity

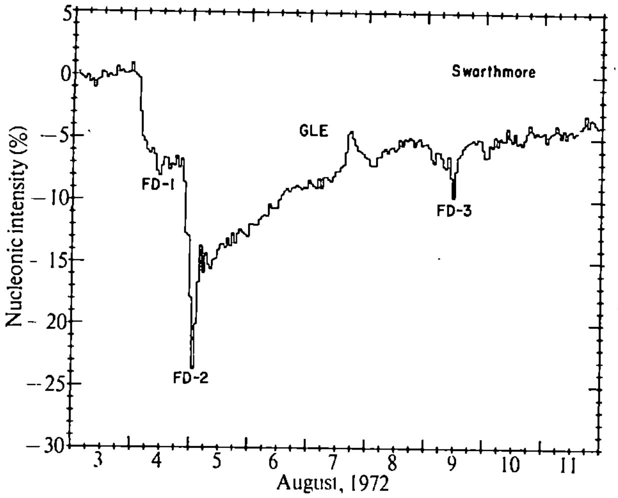

Fig. 2 Nucleonic intensity profile of the record-breaking cosmic ray storm as observed at a typical mid-latitude station (see Fig. 1).

reductions at the four stations were: Thule, 21.5%; Swarthmore, 23.7%; McMurdo, 26.8%; and South Pole, 35.2%.

The differences among the first three, all located near sea level, are a consequence of north-south anisotropy, whereas the predominant factor causing the enhancement of the effect at South Pole is the high altitude at which that station is located.

The most striking feature of Fig. 3 is the transformation of the ledge in Fig. 1 into an intensity increase GLE-1 at the polar stations. A feature of this appearance could represent either (*a*) a discontinuity in the modulation mechanism, arising from the anisotropic nature of solar plasma[6], or (*b*) the arrival of relativistic solar cosmic rays (GLE). We now examine these two possibilities, and cite the evidence leading to the tentative identification of this structure in the intensity profile as the second alternative.

The following mechanisms have been invoked in the past to account for transient intensity increases during Forbush decreases:

(1) Transient longitudinal anisotropy[7]. This effect is related to an asymmetric longitudinal distribution of the solar plasma responsible for the modulation. This mechanism would produce a phase difference between Thule and McMurdo of about eight hours, contrary to the observations (Fig. 3).

(2) Reduction in threshold rigidity[6]. The atmospheric rather than geomagnetic cutoff determines the energy threshold at the polar regions, hence an intensity increase at these stations cannot be produced by a reduction in geomagnetic threshold rigidity.

(3) Worldwide modulation. An abrupt discontinuity caused by a new shock wave overtaking a predecessor, or some other disturbance in the interplanetary medium, might produce an increase by opening a window to the outside galactic flux. At first glance, this mechanism seems attractive, as the GLE-1 maxima at both Thule and McMurdo just reached the pre-Forbush decrease level (Fig. 3). But the time resolution afforded by the recordings in two-minute intervals made it possible to determine that, for at least fourteen minutes, the cosmic ray flux significantly exceeded the pre-storm level at Thule. Furthermore, the intensity increase recorded by the South Pole nucleonic detector, which has a lower atmospheric cutoff, appreciably exceeded the pre-storm level for three hours.

These observations suggest that GLE-1 represents the arrival at the Earth of relativistic particles of solar origin. The most likely candidate for the source is an Importance 2B flare (N 15° E 09° that started on 0621 UT and ended at 0852 UT on August 4). The only dilemma with this association relates to the apparently longer than normal delay in the onset of this GLE. But the complexity introduced by the superposition of the arrival of solar particles and the modulation of the intensity of galactic cosmic rays precludes a precise determination of the onset time of GLE-1.

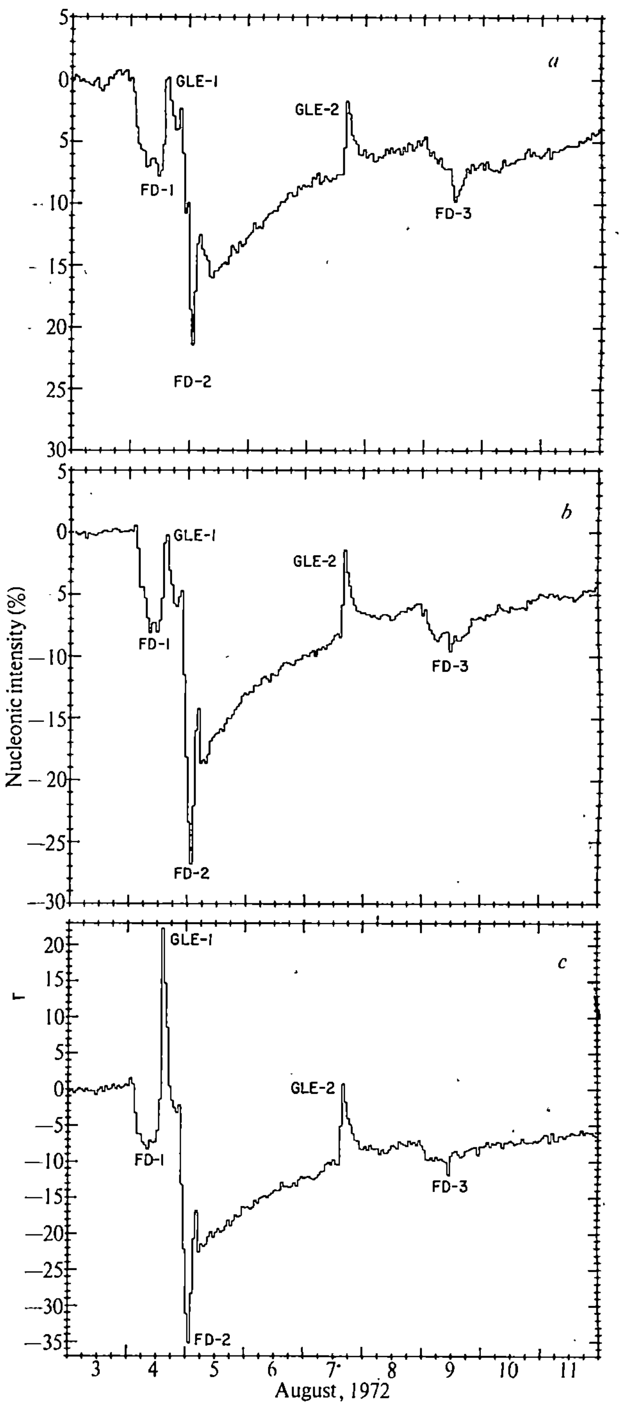

Fig. 3 Observations at the polar stations. Thule, Greenland (*a*), and McMurdo, Antarctica (*b*), are near sea level and view directions of arrival that are essentially perpendicular to the ecliptic plane. South Pole (*c*) is at an atmospheric depth of 680 $g\,cm^{-2}$, and its asymptotic cone lies at a somewhat lower latitude[3].

It is interesting to note that these observations of this great cosmic ray storm, which occurred near an epoch of minimal intensity modulation, imply that the primary cosmic ray flux in the vicinity of the Earth was cut almost in half by disturbances in a single localized region on the Sun.

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Solar Gamma Ray Lines observed during the Solar Activity of August 2 to August 11, 1972

WE report preliminary observations from OSO-7 on the emission of gamma ray lines associated with the solar flares on August 4 and 7, 1972. This is the first observation of such solar gamma rays.

The gamma ray monitor[1] consists of a shielded 3 inch by 3 inch NaI(Tl) crystal located in the rotating wheel compartment of OSO-7. Two pulse height spectra are accumulated simultaneously in the solar and background quadrants (Fig. 1) over ~90 wheel rotations in a 377-channel quadratic[2] pulse height analyser with a time resolution of 3 min. At each day/night or night/day transition of the satellite, a ^{60}Co spectrum is electronically gated into the pulse height analyser[3]. The results presented here are based on analysis of preliminary data tapes.

The 2B H_α flare of August 4, 1972, began at ~0621 UT, reaching a maximum at 0638 UT and ending at ~0852 UT (Preliminary Report SESC-PRF-Boulder 092,093). Before the satellite went into eclipse at ~0633 UT, excess gamma ray line and continuum radiation was observed. Figs 2 and 3 show a sequence of counting rate spectra which were taken before the commencement of the optical flare, during the rise of the optical flare and just after the commencement of satellite night. The live times of the summed spectra shown range from ~80→100 s. Fig. 2 shows the spectral range from ~435 to 615 keV, and Fig. 3 from ~2.1 to 2.4 MeV for accumulation in the time intervals shown. Reference to the central spectrum pairs indicates that only the solar quadrant gamma ray flux is significantly enhanced in both the ~0.5 and ~2.2 MeV spectral regions during the rise time of the optical flare. In addition, the general continuum below the line features is enhanced over the background quadrant, indicating a continuum enhancement to above 2 MeV.

A more detailed spectrum shows evidence for solar flare gamma ray line structure centred at several different energies but especially at ~4.4 and ~6.1 MeV.

Fig. 4 shows the counting rate versus time in an X-ray band (60–120 keV) and for the gamma ray lines centred at 0.5 and 2.2 MeV. The X-ray data, taken from the 4-channel X-ray detector associated with the gamma ray monitor[1], show the beginning of an increase near the time of the commencement of the reported optical flare reaching a maximum in about 5 min. The spectral features at 0.5 and 2.2 MeV begin to increase at about the same time as in the X-ray channel but with a slower rise.

The most straightforward interpretation of these observations is the near simultaneous production of nonthermal X-rays to energies greater than 2 MeV and gamma ray lines produced by a variety of high energy reactions associated with the production of solar cosmic rays. The most likely sources of the gamma ray lines are positron (β^+) production followed by annihilation (0.51 MeV), production of neutrons by solar cosmic rays followed by capture in solar hydrogen (2.22 MeV), and inelastic proton scattering[4,5]. Calculations by Shima and Alsmiller[6] and comparisons with experiments at Oak Ridge show that the gamma ray spectra produced by protons on light elements such as C and O are considerably more complex than assumed in the earlier calculations[4,6]. Thus one must be quite careful in deciding just which processes are predominant in producing the spectral features we see. We note that there may be a delay in the rise time of the enhancements shown in Fig. 4 because of the slowing down and capture times for the positrons and neutrons.

Additional evidence for the lines at 0.5 and 2.2 MeV was obtained during the 3B flare of August 7, 1972. The 3B flare began in H_α at ~1500 UT during satellite night-time. As the satellite emerged into the sunlight, excess gamma ray line radiation was observed. Figs. 5 and 6 show a sequence of counting rate spectra which were taken at night-time and during the satellite daytime period while the 3B H_α flare was still in progress.

Fig. 5 shows the spectral range from ~435 to 610 keV, and Fig. 6 from ~2.0 to 2.4 MeV for accumulations in the time intervals shown. Comparison of the lowest spectrum (night-time) with that immediately above it (daytime) shows that there are statistically significant increases in the two spectra

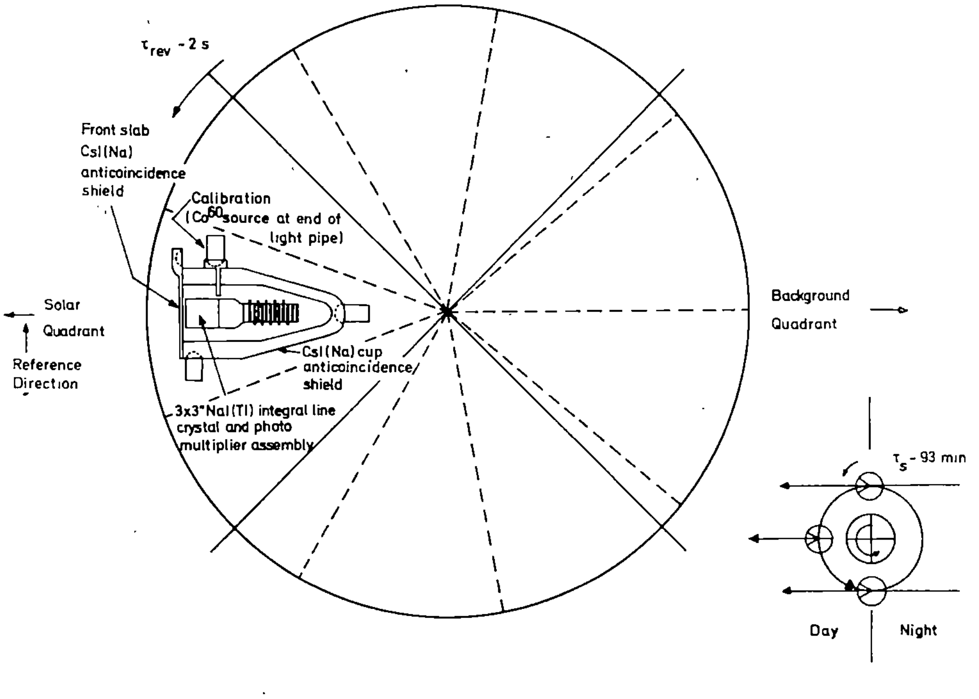
τ_{rev} - 2 s
Front slab CsI(Na) anticoincidence shield
Calibration (Co^{60} source at end of light pipe)
Solar Quadrant
Reference Direction
CsI(Na) cup anticoincidence shield
3x3"NaI(Tl) integral line crystal and photo multiplier assembly
Background Quadrant
τ_s - 93 min
Day
Night

Fig. 1 Schematic drawing of the gamma ray spectrometer, shown with the OSO wheel in the position for viewing the Sun. The solar and background quadrant identifications are also shown. The small inset at the right shows satellite aspect at sunrise and at noon and at sunset.

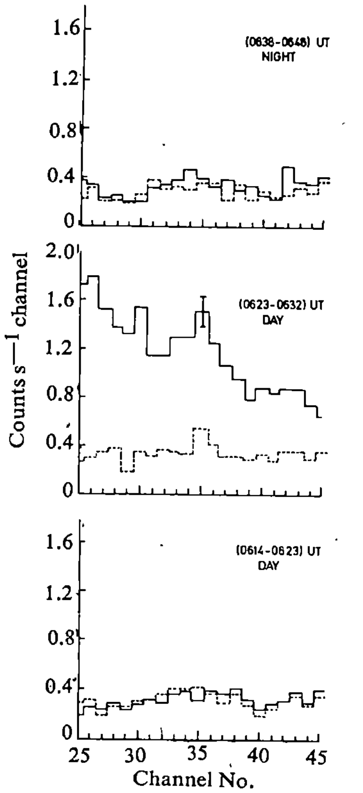

Fig. 2 The gamma ray pulse height spectrum is shown for the energy region 435 keV–615 keV on August 4, 1972. The lower spectrum was taken in the daytime before the start of the rise of the 2B Hα flare and the central spectrum was taken during the rise of the optical flare. The spectrum at the top was taken just as the satellite was occultated by the Earth. The accumulation time intervals are shown for each spectrum. ——, Solar quadrant; ----, background quadrant.

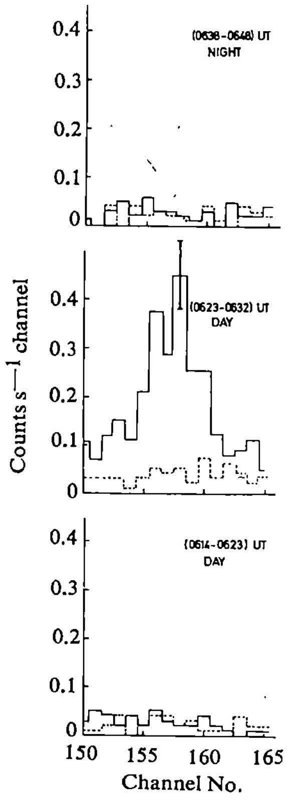

Fig. 3 The gamma ray pulse height spectrum is shown for the energy region 2.1 MeV–2.4 MeV on August 4, 1972. The lower spectrum was taken in the daytime before the start of the 2B Hα flare and the central spectrum was taken during the rise of the optical flare. The spectrum at the top was taken just as the satellite was occultated by the Earth. The accumulation time intervals are shown for each spectrum. ——, Solar quadrant; ----, background quadrant.

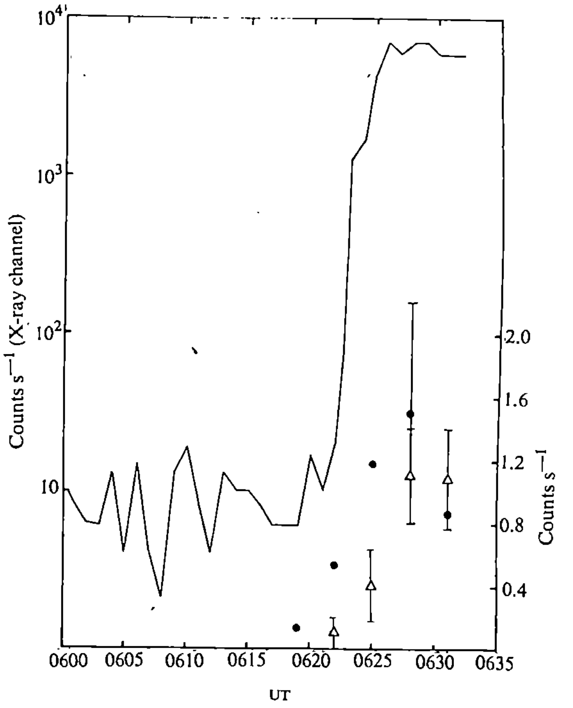

Fig. 4 The time profile (——) for the counting rate in one X-ray channel (60–120 keV) is shown covering the period of satellite day from about 20 min before the optical onset until the satellite went into eclipse. Also shown are the time profiles for the counting rates in the five channels corresponding to gamma ray lines at 0.5 MeV (●) and 2.2 MeV (△).

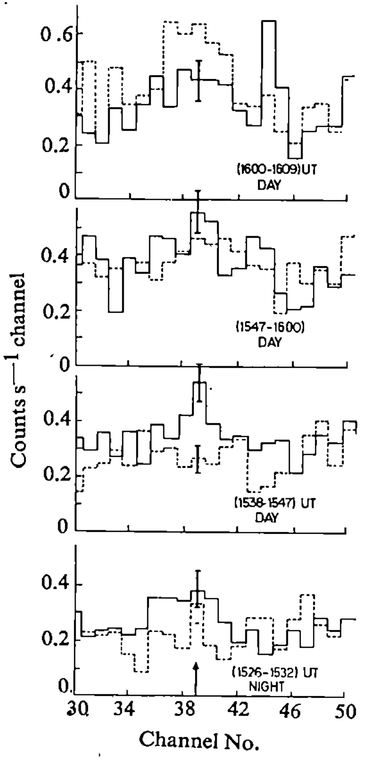

Fig. 5 The gamma ray pulse height spectrum is shown for the energy region 435 keV–610 keV on August 7, 1972. The lower spectrum was taken at night-time just before the satellite sunrise, but while the 3B optical flare was in progress. The second spectrum from the bottom was taken just after the sunrise calibration and during the declining phase of the optical flare. The top two spectra were taken at later times in the same orbit during the satellite daytime. The accumulation time intervals are shown for each spectrum. ——, Solar quadrant; ----, background quadrant.

Table 1 Tentative Designations and Preliminary Solar Flux at 1 a.u. (photons cm^{-2} s^{-1})

Associated flare and time of observations	0.5 MeV	2.2 MeV	4.4 MeV	6.1 MeV
2B (H_α) August 4, 1972, 0623–0632 UT (before H_α max)	$(7 \pm 1.5) \times 10^{-2}$	$(2.2 \pm 0.2) \times 10^{-1})$	$(3 \pm 1) \times 10^{-2}$	$(3 \pm 1) \times 10^{-2}$
3B (H_α) August 7, 1972, 1538–1547 UT (after H_α max)	$(3.7 \pm 0.9) \times 10^{-2}$	$(2.6 \pm 1) \times 10^{-2}$	$< 2 \times 10^{-2}$	$< 2 \times 10^{-2}$

corresponding to photon energies of 0.5 and 2.2 MeV respectively. In both figures the enhancement appears only in the solar quadrant spectra just after sunrise. We suggest that the enhancements here are also due to a direct solar flux, because we expect that a local satellite or atmospheric effect would produce an enhancement in both the solar and background quadrants for the detector's aspect with respect to Earth just after the night-to-day transition. The upper spectrum in Fig. 5 shows an increase in the 0.5 MeV region in the background quadrant. At this time this quadrant was viewing the Earth with good aspect but a lower rigidity ~8.0 GV, and therefore registered atmospheric radiation.

We conclude therefore that the monitor has recorded a solar burst most probably of annihilation radiation (0.51 MeV) and the deuteron formation gamma ray (2.22 MeV) in the flares on August 4 and August 7, 1972. In addition, there were solar gamma ray lines emitted during the 2B flare on August 4, 1972, most probably from excited states of ^{12}C and ^{16}O. Table 1 gives a brief summary of tentative solar flux values at the Earth for the spectral lines mentioned above in the case of both flares. For the 3B flare conservative upper limits are given for the C and O lines for the same time period.

The latter gamma ray lines are all from short-lived, excited nuclear states of the indicated nuclides and do not represent all the lines expected, but these have received considerable theoretical consideration[4,6,7].

The present observations of solar gamma ray lines are incomplete because the satellite was occulted by the Earth during the maximum of H_α emission in both flares. The observations presented here cannot eliminate the possibility that gamma rays and neutrons are produced at an undetectable level before the start of the optical flare[8]. It is tempting though to believe that these two observations in themselves give direct evidence that solar cosmic rays are accelerated in the explosive phase of the optical flare[9,10].

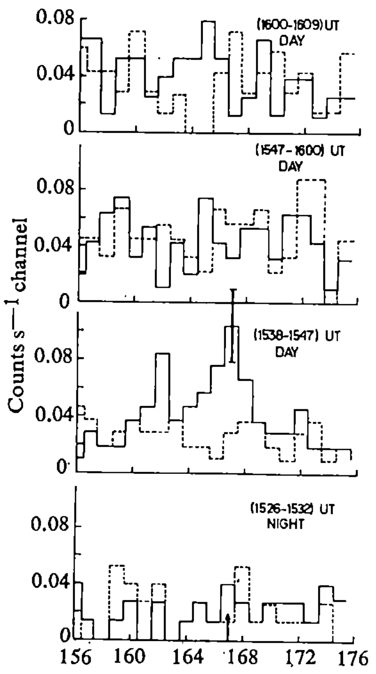

Fig. 6 The gamma ray pulse height spectrum is shown for the energy region 2.1 MeV–2.4 MeV on August 7, 1972. The lower spectrum was taken at night-time just before the satellite sunrise but while the 3B optical flare was in progress. The second spectrum from the bottom was taken just after the sunrise calibration and during the declining phase of the optical flare. The top two spectra were taken at later times in the same orbit during the satellite daytime. The accumulation time intervals are shown for each spectrum. ——, Solar quadrant; - - - -, background quadrant.

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Detection of Relativistic Solar Particles before the H_α Maximum of a Solar Flare

WE report here the first direct detection of relativistic solar protons before the H_α maximum phase of a solar flare and in near coincidence with the maximum phase of the white-light flare. These observations have important implications for theories of particle acceleration during flares and for the appropriate particle injection times to be used in the modelling of solar particle events by diffusion theories.

The time development of solar flares is frequently divided into three stages[1-5]. First, the initial phase, corresponding to local brightenings of H_α and the gradual rise of microwave radio emission and X-ray emission; second, the explosive phase, or flash phase, corresponding to a rapid increase to a maximum in the brightness and area of the flare and a rapid rise to a maximum in the width and brightness of the hydrogen H_α line; third, the decay phase, corresponding to a gradual decay of all of the flare phenomena.

Seventeen ground level solar particle events (GLE) have been observed with neutron monitors between February 23, 1956, and September 1, 1971. In the case of all the GLEs that could be associated with a flare on the visible disk, relativistic particles were first observed at the Earth (1 a.u.) with time delays ranging from $\gtrsim 5$ min to more than 1 h following the flare maximum[4]. It has been suggested that the measured radio and X-ray emissions indicate the presence of relativistic particles at the flare maximum. There have, until now, been no observations of relativistic particles at the Earth prior to, or at the same time as, the flare maximum. This has been interpreted as caused by problems of coronal and interplanetary propagation.

The ground level solar particle event of August 7, 1972, we discuss here was produced by a 3B flare in the McMath region 11976. The location of the flare was reported by the various flare patrol stations to be between W 35° and W 39°. Region 11976 was quite active as it rotated into view on the solar east hemisphere on July 30. A series of flares beginning on August 2, where the region was at ~E 30°, produced large PCA and magnetic storm effects on Earth[6]. Several smaller (1N) flares were observed in region 11976 on August 7 before the 3B flare.

A time history of the pressure corrected galactic cosmic ray rates recorded in Superneutron monitors at Sulphur Mountain (115.6° W, 51.2° N; altitude 2,283 m; vertical threshold rigidity $P_T = 1.14$ GV) and Calgary (114.1° W, 51.1° N, altitude 1,128 m; $P_T = 1.09$ GV) from August 1 to August 13, 1972, are shown in Fig. 1. The values of the solar wind speed recorded at various times by Pioneer 9 (ref. 6) are plotted at the bottom of Fig. 1. During this time Pioneer 9 was at ~0.78 a.u. and 52° east of the Earth–Sun line.

The flares of August 2 produced three shocks reported at Pioneer 9. The latter two of these shocks were observed at Earth at approximately the same time as they were observed at Pioneer 9. The first shock observed at Earth on August 4 produced a Forbush decrease beginning at ~0400 UT. A very large Forbush decrease, amounting to a galactic cosmic ray counting rate decrease of ~28% at maximum, was observed at Calgary and Sulphur Mountain on August 5. The GLE event of August 7 occurred during the recovery phase of this large Forbush decrease while the solar wind speed was slowly decreasing from the large values it was observed to have on August 4–5 (Fig. 1). A shock from the August 7 flare was reported at Pioneer 9 on August 9; at about the same time, magnetic storm activity was observed to begin on Earth, although no sudden commencement was reported[6].

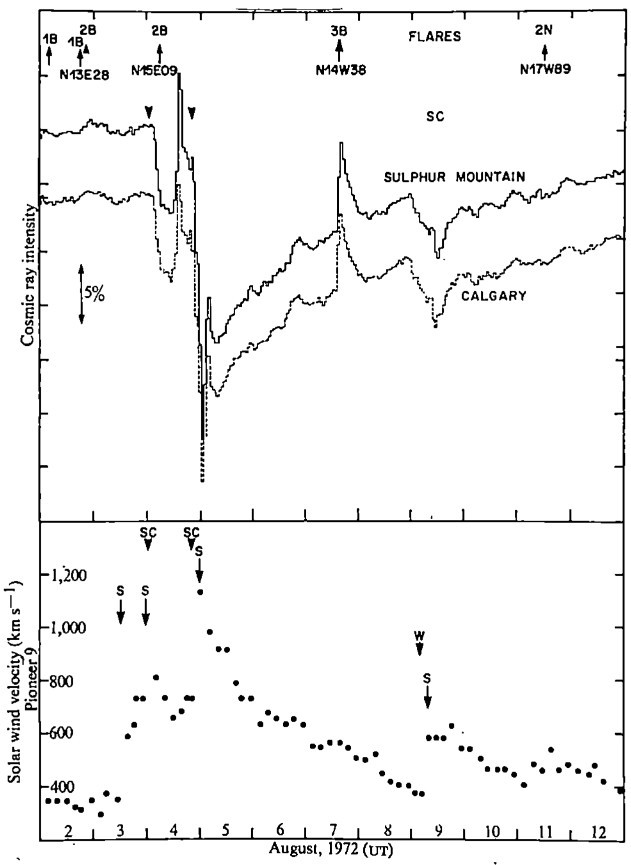

Fig. 1 Superneutron monitor cosmic ray counting rates recorded at Sulphur Mountain and Calgary for the period August 1 to August 13, 1972. Values of the solar wind speed recorded by Pioneer 9 (ref. 6) plotted at bottom. S, Shock at Pioneer 9; W, storm onset (Weston Observatory); SC, sudden commencement.

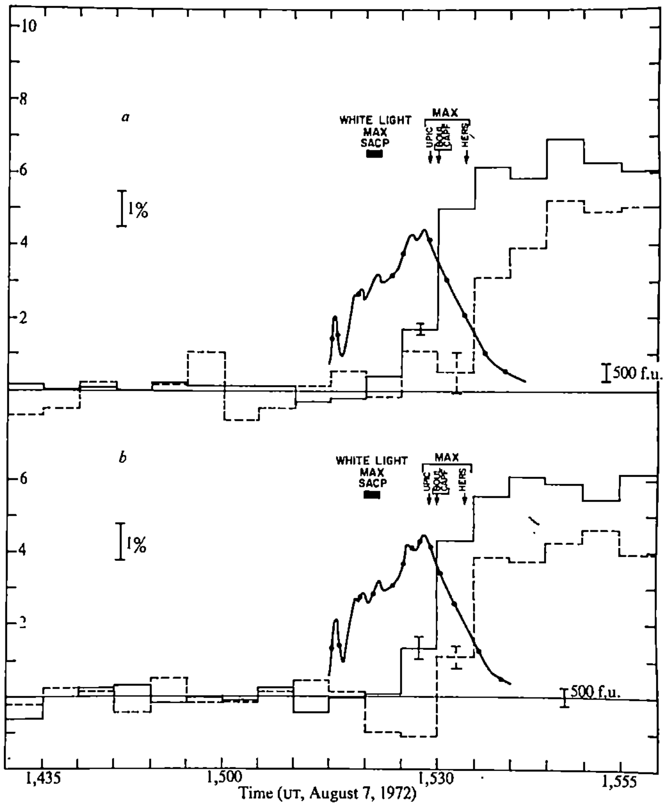

Fig. 2 5-min average cosmic ray counting rates recorded at Calgary, Sulphur Mountain, Deep River and Goose Bay in the period 1430–1600 UT on August 7. The pre-event background counting rate has been removed by subtracting a seven-point sliding average from the data. *a*: ——, Calgary; - - -, Goose Bay. *b*: ——, Sulphur Mountain; - - -, Deep River. ●—●, 2.8 GHz radio burst data from Ottawa.

We have examined the onsets of the solar particle events in the neutron monitors at Sulphur Mountain and Calgary on a time scale of 5-min average counting rates. First, the pressure corrected rates from both stations were normalized to sea-level counting rates. The galactic counting rate background during a 4 h period order before the solar event was studied. This background galactic rate was removed from the data by subtracting, from each 5-min rate, a seven-point (35 min) sliding average. This sliding average was terminated at 1510 UT and the average was then extrapolated into the period of the solar event.

5-min average neutron monitor rates from Calgary and Sulphur Mountain, with the background removed as outlined above, are plotted in Fig. 2 for the period 1430–1600 UT. The 5-min average counting rates (with seven-point sliding averages removed) from Goose Bay and Deep River are also shown. The standard deviations of the counting rates, determined from the pre-1510 UT data, are indicated for each station, and the maximum H_α flare times as reported from Pic du Midi (UPIC), Boulder (Boul), and Anacapri (CAPF) are indicated, together with the flare maximum in the calcium II line as reported from Greenwich (HERS); the white light flare maximum from Sacramento Peak Observatory (ref. 7 and D. M. Rust, private communication); and the flare observations at Ottawa at 2.2 GHz (ref. 6).

The data from Sulphur Mountain and Calgary (Fig. 2) indicate that the neutron monitors at both of these stations began to record solar flare particles in the interval 1525–

1530 UT. The counting rate increase at Calgary was ~1.7% above the background; this corresponds to an increase of ~12 standard deviations above the mean. The counting rate increase at Sulphur Mountain was ~2.3% above the background; this corresponds to an increase of ~8 standard deviations above the mean. So the counting rate increases between 1525 and 1530 UT observed at both stations are highly significant on a statistical basis and can arise only from solar particles produced in the August 7 flare.

The neutron monitor at Deep River began recording statistically significant fluxes of solar particles in the interval 1530–1535 and the monitor at Goose Bay began to respond in the interval 1535–1540. Thus, of the four stations for which data are plotted in Fig. 2, both Calgary and Sulphur Mountain first observed solar particles, with solar particles being observed at successively later times at Deep River and Goose Bay, respectively.

The data of Fig. 2 suggest that the onset of the August 7 event at Earth was highly anisotropic, as might be expected. The observed rapid onset of particles at Calgary and Sulphur Mountain and the observed anisotropy can be understood by investigating the asymptotic directions of arrival for particles of various rigidities at the four stations (Fig. 3). The location of the Sun and the direction of the interplanetary field line near Earth are shown with these data in Fig. 3. The stations at Calgary and Sulphur Mountain were within ~10° of the field line near Earth for particles of ~3–5 GV rigidity. For these particles the plot of asymptotic arrival directions indicates that both the Calgary and Sulphur Mountain monitors would be expected to observe an initially highly anisotropic solar flux before the monitors at either Deep River or Goose Bay. Also, for initial particles of this momentum, the Deep River monitor would be expected to observe the solar particles before Goose Bay. The observations (Fig. 2) and the asymptotic directions of arrival (Fig. 3) are therefore consistent with the conclusion that the initial solar flare particles had rigidities of ~3–5 GV and propagated directly to Earth along the spiral interplanetary field line.

The similarities in times of observance of the shocks of August 4 and August 9 at Pioneer 9 and at Earth suggest that the time dependence of the solar wind speed at the Earth was similar to that at Pioneer 9 during the period August 6–9. In that case, at the time of the 3B flare on August 7, the interplanetary field line between Earth and the Sun was connected to the Sun at ~W 36°±2°. So the interplanetary field provided an essentially direct connexion between the flare site and the Calgary and Sulphur Mountain asymptotic arrival directions.

The length of the spiral field line from the Sun to Earth at the time of the August 7 flare can be calculated using the solar wind speed observed on Pioneer 9 between 1500 UT on August 7 and 0400 UT on August 9. These speeds, viewed as a function of time, can be converted to a radial profile of the wind speed in interplanetary space. The time coverage of wind speed data before the August 9 shock is sufficient to determine the radial profile of the wind speed between ~0.4 a.u. (~300 km s^{-1}) and 1 a.u. (~550 km s^{-1}). We then assumed that the wind speed between the Sun and ~0.4 a.u. was a constant, equal to ~300 km s^{-1}. Using the radial profile thus obtained for the interplanetary solar wind speed, we determined an interplanetary field line length equal to ~1.12 a.u. between the Earth and the Sun at the time of the August 7 flare.

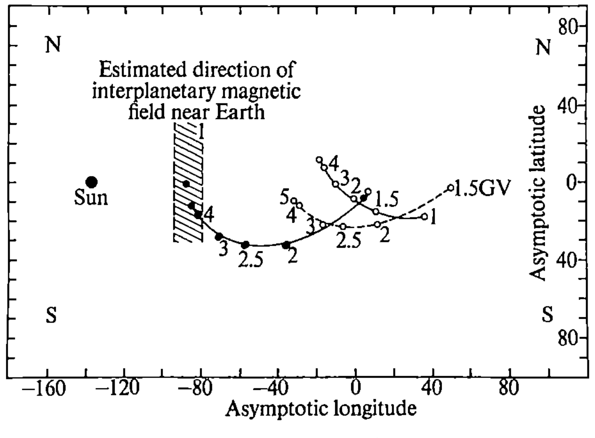

Fig. 3 Asymptotic directions of arrival[14] for relativistic particles of various rigidities incident at Sulphur Mountain, Calgary (●—●), Deep River (○ - - - ○), and Goose Bay (○—○) at 1530 UT. Location of Sun and of interplanetary field line between the Sun and the Earth also shown.

For a solar flare particle of ~4 GV momentum, $v/c \sim 0.97$. For a spiral field line length of ~1.12 a.u., the direct Sun–Earth travel time would be ~9.6 min, compared to a transit time of ~8.3 min for electromagnetic radiation. Any diffusion by these initial protons, either in the corona or in interplanetary space, would increase the travel time. Thus, the data presented here are direct evidence that relativistic protons were present on the Sun $\gtrsim 5$ min before the flare maximum as recorded by both radio and optical techniques and were present within a minute or two of the white-light maximum.

In conclusion, the observations presented here clearly show that, for this flare, particle acceleration and injection into interplanetary space occurred before the explosive (H_α maximum) phase of the flare. The near coincidence of the white-light flare and the time of particle injection supports the view that the white-light flare results from the dumping of relativistic particles into the photosphere[4]. The observations do not permit a conclusion as to whether the particles were accelerated and dumped, as well as injected, during the white-light phase[8] or whether they were accelerated before the time when they were released[9,10].

The injection of relativistic particles before the H_α maximum phase may well be a general rule rather than a special case. If so, this result has important implications for the study of relativistic solar particle propagation. In these studies, the H_α maximum is most often taken as the time of particle injection when performing fits of various diffusion models to the onset phase of a particle event (see, for example, ref. 11). If, as a general rule, relativistic solar particles are released $\gtrsim 5$ min before the H_α maximum, some of the interplanetary diffusion coefficients κ_{11} inferred in the past from the time-to-maximum t_m of particle intensities will be in error by $\gtrsim 50\%$ because $\kappa_{11} \propto t_m^{-1}$.

Our measurements were fortuitous in the sense that the asymptotic arrival directions of Sulphur Mountain and Calgary were essentially "connected" to the flare region by the spiral interplanetary field lines. Further, the interplanetary space propagation was undoubtedly aided by the existence of the Forbush decrease[12,13]. Details of the particle propagation and the implications of the measured anisotropies for coronal diffusion and transverse interplanetary diffusion will be reported later.

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Difficulties concerning a Finite Photon Rest Mass

Pecker, Roberts and Vigier have suggested that much, if not all, of the cosmological redshift might be attributable to inelastic photon–photon scattering—if the photon possesses a finite rest-mass[1]. Pecker and Vigier have attempted (private communication) to apply Vigier's ideas to the electromagnetic propagation anomalies observed by Sadeh and others[2,3]. We agree in part with the ideas of Vigier and his co-workers, but their hypothesis, as regards these phenomena, cannot be completely correct as stated.

For the case of the cosmological redshift Pecker *et al.* note that, had the photon a finite rest-mass, inelastic photon–photon scattering of extra-galactic photons on the photons of the cosmological black-body background radiation should occur. By successive interactions a photon should be progressively reddened, they claim, as it travels through inter-galactic space. They propose, in effect, a partial mechanism for the well-known "tired light" hypothesis. We have investigated the tired light hypothesis as a possible solution of the so-called "missing mass" problem[4]. It seems that the assumption of the tired light hypothesis is a workable solution of that problem. Insofar as this is the case, this solution of the missing mass problem is indirect, supportive evidence for Vigier's hypothesis.

But the mechanism of Pecker *et al.* is defective because it only partially meets the requirements of a tired light effect. Their hypothesis does not avoid the most critical problem of all non-Doppler explanations of the cosmological redshift: Olbers paradox. Although they have advanced a plausible mechanism for the reddening of individual photons, a mechanism for the reduction to the observed level of the total electromagnetic energy flux incident on the Earth from extra-galactic sources is absent. If a mechanism cannot be devised to achieve this reduction, then inelastic photon–photon scattering must be rejected as the source of the cosmological redshift. (Perhaps this difficulty might be avoided by taking the electromagnetic field to be a finite range, Yukawa type field by, for example, substituting a Yukawa potential for the Coulomb potential.)

As regards electromagnetic propagation anomalies in the solar environment, Pecker and Vigier's proposed effect is the same as that proposed for the cosmological redshift. But now the solar electromagnetic radiation field replaces the cosmic background radiation. They deduce that scattering on this field should lead to a reddening of electromagnetic radiation from planetary and stellar sources as they appear to pass near the Sun. Thus, for Sadeh's observations of the 21 cm line of Taurus A, Pecker and Vigier predict a frequency shift, the maximum shift being about 100 Hz.

Such an explanation of Sadeh's effect would be pleasing were it not for the observations carried out by Goldstein and Levy *et al.*[5,6]. They made long-term observations of the various properties of the plane-polarized, unmodulated 2.3 GHz carrier signal of Pioneer 6 as it approached and receded from occultation by the Sun. They observed several unexplained, periodically recurring transient propagation anomalies, but no long-term alterations in the signal properties that could not be ascribed to simple causes.

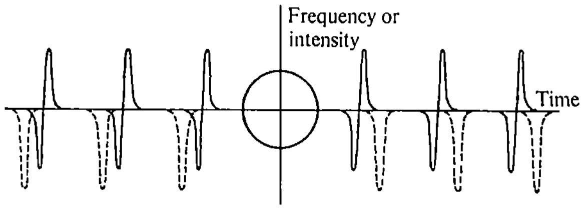

Fig. 1 Schematic diagram of the only type of propagation anomalies in the solar region consistent with the observed anomalies (refs. 5 and 6) and not at variance with other available empirical results.

To test if the various propagation anomalies are the result of an anomalous photon-graviton interaction, we have investigated to see whether transient propagation anomalies (Fig. 1) are manifested in the optical-frequency deflexion observations. The results seem to be positive[7]. Transients of this sort seem to be the only type of propagation anomalies compatible with all available observations, those of Sadeh and Goldstein included. If such transients exist, whether they are the result of photon–photon and/or photon-graviton scattering is impossible to say at present. But, irrespective of the possible existence of these transients, Pecker and Vigier's hypothesis, as currently formulated, is inadmissible on the above empirical and theoretical grounds. If inelastic photon–photon scattering takes place, the mechanism must be more complex than that advanced by Pecker and Vigier.

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Photon Mass, Quasar Redshifts and Other Abnormal Redshifts

As stated in a recent *Nature* editorial[1] "the first claims that quasar redshifts were not caused by Doppler velocities of recession were met with general disbelief". In spite of this, experimental evidence has been accumulating in favour of such non-velocity shifts (see, for example, refs. 2, 3). Burbidge (unpublished) has shown a significant anti-correlation between the apparent distance of a quasar and a nearby galaxy and the brightness of that galaxy (hence a correlation with its distance): this suggests a physical association, in many cases, between two objects, a QSO and an ordinary galaxy, displaying very different redshifts.

Here, we discuss the application to quasars of a mechanism[4] which provides a simple explanation of the essential observational paradoxes which have prevented a coherent understanding of the nature and distance of QSO sources.

The new mechanism rests on the possible existence of a non zero photon mass $m_\gamma < 10^{-48}$ g. We prefer this mechanism to others (such as Hoyle and Narlikar's[5]) because this one explains not only the QSO redshifts but several other phenomena, with the same value of the phenomenological constant of our formula.

Flato and Vigier (unpublished) show how one can generalize to photon–photon interaction from an interaction scheme discussed by Corben and Schwinger[6] for spin 1 mesons; we introduce inelastic photon–photon collisions which yield a constant fractional energy loss cross section independent of the photon energy, have a very strong forward peak and do not invalidate quantum electrodynamics, provided one utilizes suitable form factors which drop sharply off the mass shell.

In other words, a background transverse photon exchanges a virtual longitudinal photon (in its rest frame) with an incoming transverse photon and produces a soft transverse photon pair. This implies that transverse photons crossing a transverse radiation field lose energy according to the law

$$\delta z = \delta p/\gamma = -\int c U(\rho) \mathrm{d}\rho \qquad (1)$$

where $U(\rho)$ represents the photon density, $\mathrm{d}\rho$ the distance therein and c a constant which should be determined by experiment. This theory might somewhat modify our ideas concerning the expansion of the Universe. So far, we claim only that, in addition to the cosmological redshift, there exists, particularly strongly in quasars, another source of redshift, the photon–photon interaction. As to the expansion, we think that a revision of the Hubble–Sandage scale is not to be ruled out, on the basis that usual determinations assume more or less an identity in physical properties for close by galaxies and for the most remote ones: for example, why should the absolute size of H II regions be the same for young and old galaxies? We have indeed some good reasons to believe the contrary. In that case, an increase of the Hubble constant from 50–100 km s^{-1} Mpc^{-1} to 100–200 km s^{-1} Mpc^{-1} would bring back the cosmological temperature derived from our value of A to a value compatible with both expansion and photon–photon interaction. We note that our interpretation does not modify the classical interpretation of Olbers paradox: any source of redshift, cosmological or not, would give the same solution. In a blackbody radiation field equation (1) becomes

$$\delta t = -\int A T^3(\rho) \mathrm{d}\rho \qquad (2)$$

where T represents the background temperature and A a phenomenological constant.

We can determine the constant A by using measurements of redshifts in some conditions better known than those in QSOs.

We have found that the value determined for A, from different astrophysical observations, is: (i) Redshift of the Fraunhofer lines at the disk limb of the Sun, as measured by Roddier[8]

$$0.6\times10^{-29} \leq A \leq 3\times10^{-29}\ \mathrm{K}^{-3}\ \mathrm{cm}^{-1}$$

These measurements are impossible to interpret as the result of any other effect[9]. Snider[10], using other lines, did not find this effect, but it seems to us that Roddier's experiments have a better accuracy, (ii) redshift of the 21 cm line of a radio source occulted by the solar atmosphere[11,12]

$$1.4\times10^{-29} \leq A \leq 7\times10^{-29}\ \mathrm{K}^{-3}\ \mathrm{cm}^{-1}$$

(iii) If we interpret the Hubble redshift as due to, at least in part, the effect we invoke, it gives indeed an upper limit to A; if the Hubble constant $H_c = 50$ km s^{-1} Mpc^{-1}

$$A \leq H_c/T^3 = 2.7\times10^{-30}\ \mathrm{K}^{-3}\ \mathrm{cm}^{-1}$$

assuming $T = 2.7$ K for the cosmological radiation field. To obtain a value of A consistent with (i) and (ii) we require, say, $T = 2.2$ K and $H = 100$; we would then get $A \leq 10^{-29}$. The accepted value of the Hubble constant may be questioned, which would completely reconcile the observed value of 2.7 K for the cosmological temperature and our limits for A, provided $\mathrm{H} \gtrsim 180$ km s^{-1} mc^{-1}. The Hubble constant has recently been revised downwards taking into account, notably, the size of large H II regions. This size may be a function of the degree of evolution of the galaxy, through the stage of quasars[13], so the more recent evaluations of the Hubble constant may have been incorrectly biased, and we feel that the value 200 km s^{-1} Mpc^{-1} is not to be ruled out.

Our mechanism adds two astrophysical processes to the well known sources of redshifts, both consequences of the photon–photon interactions: first, a redshift associated with the travel of photons from a remote source to the observer, through the interstellar microwave field of 2.7 K or so; second, a "source" redshift associated with the existence of a photon bath surrounding radiating sources—which can be small (Sun) or extended (some galaxies, quasars); if R_s is the radius of the radiating source, the effect is of the order of

$$\delta z \simeq -A\ T_s^{-3}\ R_s$$

assuming a blackbody radiation field for the source.

If one accepts the observed z values as reflecting true distances (from expansion theory) quasars should have luminosities a hundred or a thousand times brighter than those of normal galaxies. The existence of usual carbon and magnesium lines at such energies is very difficult to understand. Further QSOs are evidently condensed objects (with $R_s \lesssim 1$ pc). From the observed time variation of their optical and radio brightness it seems that the regions which produce the observed energy have a maximum diameter of a few light day ($R_s \sim 10^{15}$ -10^{16} cm); it is difficult to construct energy generation mechanisms that could work under such restrictions. Successful attempts have been made, but they seem to us rather artificial and *ad hoc*. The situation is different from our point of view. If the essential part of QSO redshift results from the slowing down of emitted photons by the radiation field surrounding the source, one explains immediately Arp's empirical observation[3] that QSOs are associated with nearby galaxy chains and clusters and seem to avoid all distant systems of galaxies. QSOs become "normal" objects: the distribution in the sky of QSOs of the brightest apparent magnitude is associated with the local group of galaxies; the distribution of fainter QSOs is associated with more distant but still nearby galaxies in the local supercluster.

We suggest that QSOs are extended structures, with massive cores and a relatively high average temperature, and surrounded by a transparent region, where the size of the photon bath has the same order of magnitude of the size of the QSO ($10^{15} \leq R_s \leq 10^{16}$ cm). The temperature we assume for the QSO core or cores is about $10^4 < T_s < 10^5$ K, a range of values derived from the observed blue colours of these sources.

With $A \sim 2\times10^{-29}$, $T_s = 2\times10^4$ and $R_s = 5\times10^{15}$ the obtained value for z, according to equation (2), will be 0.8, a sensible average value for QSOs.

Because z essentially results from variations of the surface radiation temperature we expect that if our assumption is correct we should observe something like a Gaussian distribution of the numbers of QSOs around this average equilibrium value T_s. To test this, the best method is to plot the number N against the values of T according to equation (1). This can be done by transforming the empirical curve $N(z_\gamma)$ established by Roeder and Dyer[14] which takes into account the probable effects of the terrestrial atmosphere on QSO redshift measurements. Starting from the best fit curve of Fig. 1, we obtain the curve $N(T)$ by the cubic root of the z_γ values of Fig. 1. This yields indeed a symmetric curve peaked around the value $T_{\mathrm{Q}} \sim 10^4$ K.

We have accepted here the argument of Roeder and Dyer that the curve has only one maximum, the two other observable maxima resulting from observational bias. If it turns out that there exist other real peaks (such as the apparent peak around $z_\gamma = 2$), these could be interpreted as corresponding to other types of objects differing by the equilibrium temperature, that is, by the extent of the ionization regions to part or all of the young galaxy which we suggest is a QSO. Further, the cutoff of N for $z_\gamma > 2.3$ results naturally from our model. Values

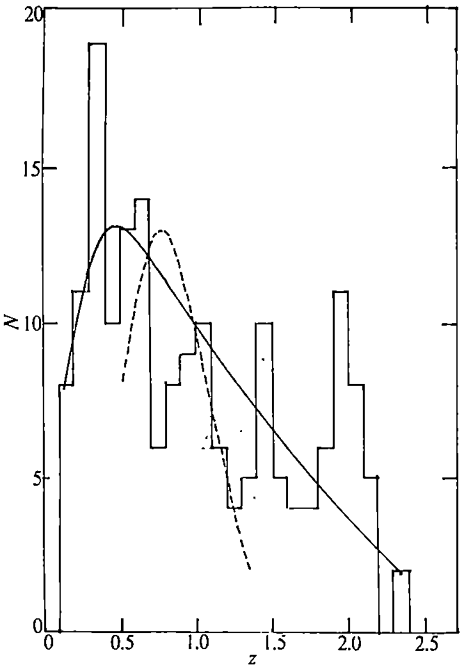

Fig. 1 The distribution of 178 quasar emission line redshifts together with the smoothed distribution (——) of Roeder and Dyer. The dashed line (- - -) corresponds to their distribution with $Z^{1/3}$ proportional to T.

of $z_\gamma > 2.3$ are not probable. Because we are observing only a finite set of QSOs in our local supercluster and no observations are yet possible in the other superclusters the cutoff reflects the limited nature of the observable sample.

The fact that the value for z_γ, z_γ(obs), deduced from absorption lines, approximately coincides with the z_γ deduced from emission features is also natural if one assumes that the emission and absorption both take place near the emitting core or cores of the QSO, as in the model recently proposed by Schmidt[15] which yields for the average value of the QSO mass $5 \times 10^{12}\ M_\odot$. This is consistent with the description of QSOs as young galaxies.

A simple independent quantitative analysis of typical QSO energy balances strongly supports this model. In order to fit the brightest QSO in apparent magnitude (3C 273) in an observed galaxy chain one must reduce its distance by about a factor 10^2. It thus radiates 10^{43} erg s^{-1} (instead of the generally assumed 10^{47}) which corresponds to a surface flux of $F_{QSO} = 10^{43}/(4\pi \times 10)^{30} \sim 10^{12}$ erg s^{-1} cm^{-2}. The solar surface flux $F_\odot = 10^{33}/(4\pi \times 36 \times 10)^{20} \sim 10^{10}$ erg s^{-1} cm^{-2}. The surface temperature of the QSO core or cores is thus $\sim 10^{40}$ K in good agreement with our determination.

If QSOs are young galaxies with a condensed central core, or cores, whose surface produces the observed emissions and with a rather hot surrounding "bath" of photons corresponding to an average temperature of 10^4 to 10^5 K, and they are almost normal objects, containing the usual elements observed in the "cooler" older type of galaxies, then there exists, in Arp's words, "a continuity of physical characteristics going from quasars through compact galaxies to companion galaxies".

We suggest that, as a consequence of differences of temperature of their radiation field, QSOs seem to have larger redshifts but companion galaxies also have higher redshifts than the accompanying galaxies because they are in a "hotter" younger form. Their formation is linked to the earlier stages of the evolution of the protogalaxy towards a normal galaxy through a production mechanism of the type suggested by Pecker[13].

Further, QSOs do not belong to an autonomous very distant population of objects but are generally associated with galaxy chains and clusters observed in the same direction. This means that their "true" distance is from 10 to a 1,000 times smaller than is generally assumed at present. This suppresses many difficulties; (because the total energy produced is reduced, the known pairs of sources as in 3 C 379 which seem to separate at velocities of the order of 10*c* are at least 10 to 100 times closer than we thought, and strange anomalies such as the large apparent radii of some quasars (discussed by Miley and quoted in ref. 3) disappear.

In our model, the process of galaxy creation is such that QSOs, compact galaxies, blank field radio sources, luminous material, lines of galaxies and companion galaxies result from ejection in opposite directions from the nuclei of large young galaxies. Spiral galaxies, galaxies which are ejecting or have ejected material in opposite directions, would naturally contain a hotter radiation field than amorphous elliptical galaxies; so that Jaakala's results[2] are also encompassed by our new redshift mechanism.

Finally, in this model the radio-emission by QSOs is due to the long wavelength component of the spectrum emitted by the photon–photon interactions. A photon from the source collides with a photon from the field and they produce a group of three types of particles: two very low (radio) energy photons, a reddened photon, and the perturbing photon. The theory of the radio-emission must be derived from the theory of photon–photon interaction; but clearly it will not produce a thermal radio-spectrum.

Although, in this construction, each argument taken separately may not be entirely convincing, we feel that a set of converging arguments gives our views an exceptional coherence, and a larger amount of credibility than other theories.

We thank Professor Papapetrou, Dr J. Madore and C. Dyer for helpful discussions.

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Comment on "Non-Velocity Redshifts and Photon-Photon Interactions"

IT has been claimed recently[1] that some redshifts can be explained by considering a new type of process in which the incident photon scatters inelastically on the 3K radiation to give four less energetic photons. The Lagrangian responsible for the interaction is taken as $\Lambda(A_\mu A^\mu)^2$ and the process is considered in the second order only to account for the necessary

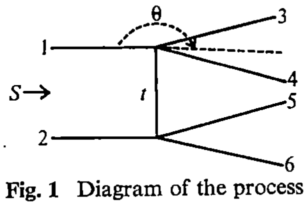

Fig. 1 Diagram of the process.

strong peaking of the cross-section (see Fig. 1). Here we describe the detailed calculation of this process

The differential cross-section is given by

$$\mathrm{d}\sigma = \frac{1}{4\,\omega_1\omega_2}\,|\mathcal{M}|^2(2\pi)^4\delta^4(p_1+p_2-\sum_{i=3}^{6} p_i)\prod_{i=3}^{6}\frac{d^3P_i}{(2\pi^3)\,2\omega_i} \qquad (1)$$

where ω_i and p_i are the energies and momenta of the external photons. The invariant matrix element $\mathcal{M}$ is given in terms of the polarization vectors ε^i and the exchanged momentum squared t by

$$\mathcal{M} = 64\,\Lambda^2\,\varepsilon^1_\mu\varepsilon^3_\rho\varepsilon^4_\sigma(g^{\mu\varrho}g^{\sigma\lambda}+g^{\mu\sigma}g^{\lambda\varrho}+g^{\mu\lambda}g^{\sigma\varrho})\,\frac{g_{\lambda\tau}}{t}\,\varepsilon^2_\alpha\varepsilon^5_\beta\varepsilon^6_\gamma\,(g^{\alpha\beta}g^{\gamma\tau}+g^{\alpha\gamma}g^{\beta\tau}+g^{\alpha\tau}g^{\beta\gamma}) \qquad (2)$$

Averaging over polarizations yields

$$|\mathcal{M}|^2 = \frac{72\,(64\;\Lambda^2)^2}{t^2} \qquad (3)$$

Putting $(p_1+p_2)^2=S$, $(p_3+p_4)^2=\mu^2$, and $(p_5+p_6)^2=\mu'^2$, one gets in the centre-of-mass frame for $\mu^2,\mu'^2 \ll S$

$$\frac{\mathrm{d}\sigma}{2\pi\mathrm{d}\cos\theta\,\mathrm{d}\omega_3\mathrm{d}\omega_4} = \frac{1}{4\,\omega_1\omega_2}\,|\mathcal{M}|^2\,\frac{1}{(4\pi)^6}\,[\omega_3^2+\omega_4^2+\omega^2+2\omega_3\omega_4-2\omega_3\omega-2\omega_4\omega]^{-1}\,\frac{1}{|f'(\omega)|}\,\mathrm{d}\mu^2\,\mathrm{d}\mu'^2 \qquad (4)$$

where $f(\omega)=\omega_1+\omega_2-\omega_3-\omega_4-\omega-[\omega_3^2+\omega_4^2+\omega^2+2\omega_3\omega_4-2\omega_3\omega-2\omega_4\omega]^{1/2}$

$$f'(\omega) = \frac{\partial f}{\partial\omega}$$

and ω is the positive root of $f(\omega)=0$ (if it does not exist $\mathrm{d}\sigma=0$). θ is the scattering angle for the quasi-elastic process.

A simple integration over μ^2 and μ'^2, restricting μ^2 and μ'^2 to values less than K (small compared to S), gives

$$\int_0^K\int_0^K \frac{\mathrm{d}\mu^2\,\mathrm{d}\mu'^2}{t} \sim \frac{4}{\cos\theta}\int_0^{\frac{2K^2}{S^2}\cos\theta} \mathrm{d}X\log\left(\frac{K}{S}\sqrt{\frac{2\cos\theta}{X}}\right)[1-\cos\theta+X]^{-2} \qquad (5)$$

which behaves as $-\dfrac{2}{1-\cos\theta}\log(1-\cos\theta)$ when $\theta\to 0$.

Consequently such a process does not lead to strong peaking in the forward direction, which is necessary in order to get a point-like image of the source. (In the laboratory frame the angular dispersion is reduced merely by a factor of 0.5.) Moreover, it is obvious from equation (4) that there is no well-defined redshift independent of the frequency of the incident photon. Instead, because the cross-section is an algebraic function of the final energies, the frequency response is predictably spread all over the available phase-space, giving grey radiation rather than a shifted line.

We therefore conclude that this process cannot account for any observed redshift.

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Photochemical Ozone Formation in the Atmosphere over Southern England

ATKINS *et al.*[1] present evidence of photochemical ozone formation in the atmosphere over southern England. When, however, the diurnal ozone variation is carefully examined, some doubt may be felt whether all the ozone measured was indeed locally generated. The data given by Atkins *et al.* include thirteen days where pronounced ozone peaks could be observed and in all these cases the maxima occurred in the late afternoon, between 1600 and 1700 BST. These late afternoon maxima are not in accord with the predicted diurnal variation of photochemically produced ozone; the daily maxima should appear between 1200 and 1400 local standard time, when the combination of high insolation and temperature leads to enhanced ozone production[2].

Continuous ozone and oxidant measurements performed in Los Angeles[3], Aspendale, Australia[4], and Jerusalem[5] demonstrate that peak concentrations do indeed always occur soon after local noontime. Fig. 1 shows the detailed variation of oxidant concentration, insolation and vehicle density (at the site of measurement) in Jerusalem for a typical day in July. The vehicle density was approximately constant and the oxidant concentration curve follows the insolation curve with a displacement of two hours at most. The Los Angeles data[3] exhibit the same behaviour exactly.

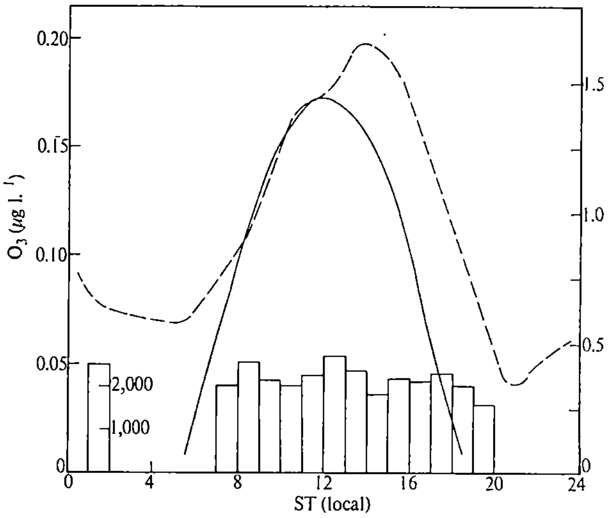

Fig. 1 Diurnal variation of oxidant concentration, insolation and vehicle density. Oxidant concentration is given by μg l.$^{-1}$. - - -, Ozone concentration; ——, insolation.

If all the ozone recorded at Harwell were produced locally by photochemical reactions, the same diurnal pattern would be expected. The discrepancy between the expected and observed pattern may be explained in part if the relevant meteorological conditions are taken into account. Synoptic data for July 3, 1971, show the existence of a low inversion (700 m), high surface temperature and pressure and weak winds, conditions leading to elevated pollutant concentration over southern England. For July 7 meteorological data are not given, but from the daily weather report of the British Meteorological Office we found that conditions were again favourable for increased ozone production. On the other hand on June 26 synoptic data show high inversion, low pressure and temperature and westerly winds. The ozone values were much lower, and the maximum appeared at about 1400 BST.

Because photochemically produced ozone should attain its highest concentration in the early afternoon, it seems clear that some other mechanism is responsible for the delayed maxima measured at Harwell. We suggest that these maxima are due not only to increased local production but also to advection of ozone from the London Metropolitan area, where ozone generation was also enhanced, as the same meteorological conditions prevail at both places.

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Elevated Ozone Levels in the Air of Central London

Among the reactions of primary pollutants with one another and with substances naturally present in air, the reactions induced by light are particularly important. The occurrence of such reactions is related to the accumulation of strongly oxidizing species, particularly ozone[1], which occurs naturally in the atmosphere to the extent of 20–50 p.p.b. during daylight[2,3]. Ozone can be detected by smell by sensitive individuals at 100 p.p.b.[4], which value is a suitable threshold for an air quality evaluation, having been proposed as an air quality standard in the USA[5].

Table 1 Ozone and Meteorological Data for July 12 to 14, 1972

Ozone concentrations:	July 12, 1972	July 13, 1972	July 14, 1972
Maximum value (p.p.b.)	99.6	112.0	102.2
Maximum hourly average (p.p.b.)	85	111	83
Mean daily concentration (p.p.b.)	33	43	38
Number of minutes above 100 (p.p.b.)	0	250	10
Meteorological data for Kew, London, at mid-day[6]			
Wind speed, knots	5	0	7
Temperature, °C	21	22	23
Dewpoint temperature, °C	9	9	12
Visibility, km	20	11	11
Number of sunshine hours	13.2	10.2	13.0

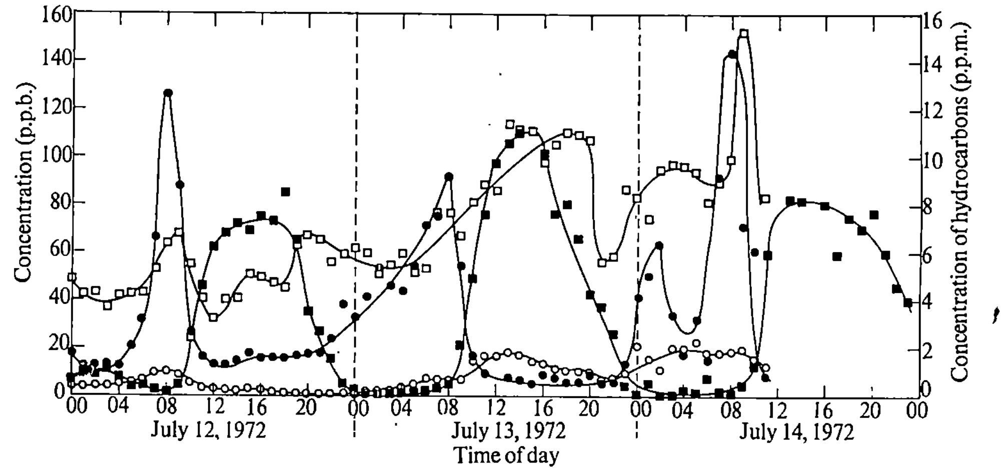

Fig. 1 Diurnal variations of air pollutants measured in London from July 12 to July 14, 1972. ■, Ozone, p.p.b.; ●, nitric oxide, p.p.b.; □, nitrogen dioxide, p.p.b.; ○, hydrocarbons, p.p.m.

This laboratory is currently monitoring the air quality in respect of a number of pollutants at its laboratory in Endell Street, Holborn, London. The pollutants include ozone, nitric oxide, nitrogen dioxide, carbon monoxide, total gaseous sulphur compounds and total gaseous hydrocarbons. The sampling point is away from traffic and is not influenced by a specific pollutant source; it is representative of the background air in Central London.

The concentration of ozone measured from July 12 to 14, 1972, at this site is given in Table 1 together with the meteorological data for these days. The diurnal variation in the concentration of ozone and other pollutants during July 12, 13 and 14 is shown in Fig. 1. The variation in concentration of the pollutants during daylight is typical of photochemical processes[4]. Values for ozone concentrations in excess of 100 p.p.b. were first recorded in the United Kingdom at Harwell, Berkshire, on July 3, 1971, and July 7, 1971 (ref. 7). The ozone concentrations now reported are higher and represent the first measurement of photochemical air pollution in a British city.

The weather conditions which lead to the formation of photochemical air pollution include sunlight and light wind or calm conditions. We find at midday on July 13, 1972, and July 14, 1972, and July 3, 1971, at Harwell, wind speeds were force 2 or less, cloud cover was 2/8 or less and temperatures were 18° C or more.

A search of meteorological records for the past ten years has shown that the above conditions prevailed at midday at Heathrow, London, on 15 occasions in the months April to September (J. Briggs, private communication). Consideration of the rate of increase in the ozone concentration on July 13 in the period between 1000 h and 1600 h (28 p.p.b. h^{-1}, Fig. 1) would indicate that two hours of suitable meteorological conditions in this period would be sufficient to cause the ozone concentration to exceed 100 p.p.b. at present levels of nitric oxide and hydrocarbon emission. Data on the frequency of such periods are not immediately available.

On July 25, 1972, there was 4/8 cloud cover at midday but this had decreased to less than 2/8 by 1300 h. The ozone concentration rose and had exceeded 100 p.p.b. for 20 min by 1600 h. The wind speed was less than force 2 and the temperature over 18° C as before.

Measurements are continuing and a more detailed discussion will be presented later.

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BIOLOGICAL SCIENCES

Papova Virus in Urine after Renal Transplantation

THE excretion of viruses of the papova type in urine following renal transplantation has been described only in a single case[1]. Excretion of herpes viruses is more common, and a high incidence of warts in transplant patients has also been reported[2]. A papova-like virus has been found in brain material of patients with progressive multifocal leucoencephalopathy (PML) and such viruses have been cultured from cases of PML complicating Hodgkin's disease[3,4]. Immuno-suppressive therapy activates latent viruses[5] and is associated with a high incidence of malignant tumours[6]. We report here the excretion in urine of a papova-like virus by approximately 45% of patients in a renal transplant unit.

The patients (Table 1) had received renal allografts between thirteen and twenty-two months before the start of the investigation. Thirteen patients received kidneys from dead donors, four had kidneys from living donors, while one patient received a second kidney (from his mother) after removal of a rejected kidney from a dead donor. The standard immuno-suppressive maintenance therapy consisted of irradiation (150 rad) on days 1, 3 and 5 after transplantation, azathioprine ('Immuran'), prednisolone and horse antilymphocyte serum (Behringwerke).

Urine specimens from transplant patients were taken at weekly intervals, and samples from eight staff members of the transplant unit were investigated at least once during the period of June 21, 1972, to August 1, 1972. Urine (12 ml. aliquots) was centrifuged within 1 hour of collection at 32,000 *g* in a 'Beckman model A' centrifuge ('type 40' rotor) for 1 hour. The pellet was resuspended in 12 ml. distilled water, and centrifuged in the same way. The supernatant was decanted and the pellet used for electron microscopy. Samples of antilymphocyte serum (1 ml.) used in the treatment of the patients were made up to 12 ml. with distilled water and examined for virus particles in the same manner. Serum and virus positive urine pellet from patient CD11 was used for immune electron microscopic studies.

Table 1 Patients and Detection of Virus Particles

Patient	Age and sex	Date of transplant	Date of virus detection	Virus diameter (nm)
CD4	40 (M)	September 17, 1970	July 5, 1972 July 18, 1972	45±0.4
CD6	44 (F)	November 24, 1970	June 28, 1972	48 *
CD11	58 (F)	July 15, 1971	June 28, 1972 July 18, 1972 July 24, 1972	43±1.7
CD14	28 (F)	October 3, 1971	July 24, 1972	47±1.9
CD18	49 (M)	March 3, 1972	June 28, 1972 July 18, 1972	48±1.6
CD2–LD3	32 (M)	April 11, 1970 May 7, 1971	July 24, 1972	43 *
LD2	15 (M)	January 15, 1971	August 1, 1972	43 *
LD5	38 (F)	March 1, 1972	August 1, 1972	43 *

CD = Patient received kidney from dead donor.
LD = Patient received kidney from living donor.
* = Insufficient particles (less than 4) for s.e. determination.

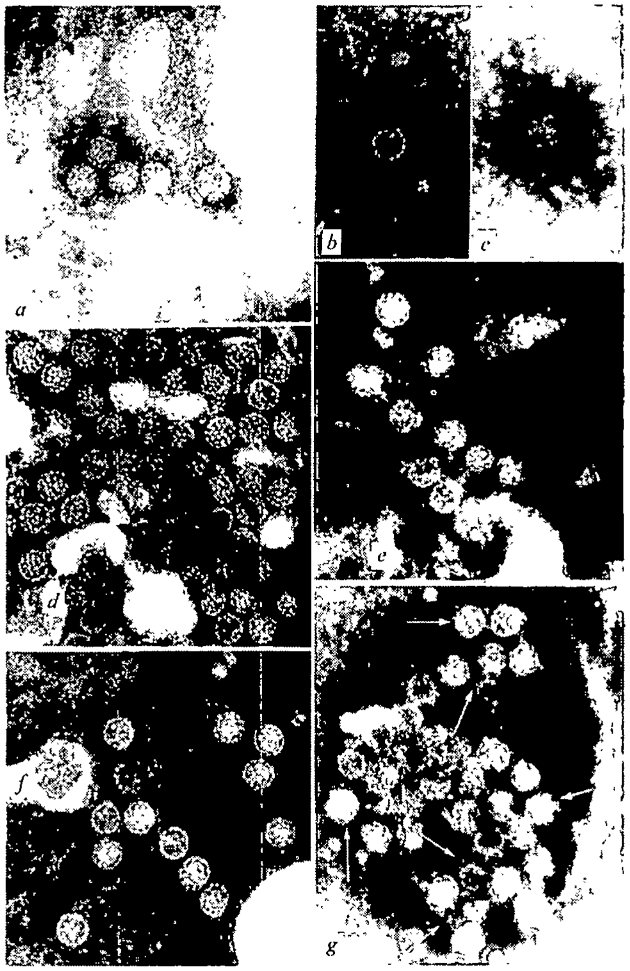

Fig. 1 *a–f*, Papova-type virus particles. A small portion of the pellet from centrifuged urine samples was taken up in a drop of distilled water and this suspension mixed with a drop of 3% (w/v) phosphotungstic acid at *p*H 6. A drop of this mixture was put on to a 'Formvar'-carbon coated grid, the excess fluid removed with filter paper and the grid allowed to dry. Preparations were examined in a 'Siemens Elmiskop 1A' electron microscope at 80 kV at ×40,000. Particle diameters were measured on negatives employing a 'Nikon model 6C' comparator. The figures *a–f* correspond to the virus positive patients CD4, CD6, CD6, CD11, CD14 and CD18 respectively as shown in Table 1. ×96,000. *g*, Immune electron micrograph. Serum from patient CD11 taken on June 14, 1972, was diluted 1 : 4 in distilled water. A portion of the pellet obtained from her urine was mixed with a drop of the diluted serum, stained and examined as before. Note clustering of antibody-coated virus particles. Viral antibody indicated by arrows. ×96,000.

Details of the patients, dates of transplants, dates of initial and subsequent virus detection and virus particle size are given in Table 1. Particles with the typical morphology and size of the polyoma group[7] were seen in the urine of eight (44%) of the patients (Fig. 1*a–f*). The concentration of virus present varied from patient to patient, some showing only a few particles while patient CD11 excreted the largest number of particles (Fig. 1*d*). Three of the patients were virus-positive on more than one occasion. The particles correspond in size to the polyoma-SV40 sub-group[7] and have the typical morphology. Those particles showing slightly larger diameters presumably represented partially collapsed capsids.

Patient CD11 excreted a herpes-type virus and was subsequently found to be positive for cytomegalovirus. One of the papova-negative patients was found to excrete an unidentified icosahedral virus particle having a diameter of approximately 53 nm, but the morphology of this particle did not resemble that of the papova group. Polyoma virus is characterized by the presence of aberrant tubular forms of the capsid[7]; the absence of these in our investigations suggested that the particle is more like SV40 which lacks such tubes. Urine of eight staff members working in the unit contained no virus and no particles were observed in the antilymphocyte serum. The serum of patient CD11 whose urine contained the largest number of particles was shown to contain antibody against them (Fig. 1*g*). Antilymphocyte serum preparations did not contain antibody.

The fact that there was no apparent correlation between virus occurrence and date of transplant in the patients suggested that virus excretion occurred at intervals depending on antibody status. Regular screening of urine specimens should provide information in this respect. The form of immunosuppression given may be significant, supported by the fact that the patient of Gardner *et al.*[1] does not appear to have received any antilymphocyte serum. It is interesting that approximately 150 urine specimens from 31 kidney transplant patients examined by one of us (G. L.) during 1971 at Hammersmith Hospital, London, contained no papova-like particles. These patients, too, received no antilymphocyte serum. In a separate study, electron microscopic screening of urine from an equivalent number of Hodgkin's patients (18) not receiving antilymphocyte serum has yielded negative results with respect to papova-type particles so far.

The particles found in the present investigation seem to be similar to the "B.K." virus of Gardner *et al.*[1], which is substantiated by their size and morphological characteristics. Work on the culture and serology of the virus is in progress, in order to compare it with that found in cases of PML[3].

Our patients have limited contact with each other and because no virus particles could be found in urine from staff of the kidney unit it was likely that the virus represented a latent human virus activated by immunological means[5]. The high incidence of virus-positive patients is worthy of note. We consider it remarkable that the polyoma-type particles are significantly more prevalent than other cubic virus forms which suggests that, if this is not fortuitous, then presumably a delicate balance in the immune system has been disturbed which has favoured the multiplication of this virus.

Follow-up of these patients may yield information about a possible relationship between virus excretion and the development of malignant tumours[6]. Experiments to determine the ability of the virus to transform cells and its possible oncogenic potential are envisaged.

We thank Dr W. H. F. Kenny (H. F. Verwoerd Hospital), Dr K. E. Weiss (Veterinary Research Institute, Onderstepoort) for facilities provided and Professor J. N. Coetzee for his comments.

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Diploidy and Chromosomal Structural Hybridity in *Phytophthora infestans*

IN the midst of some controversy, cytological and genetical evidence is accumulating to support the view that, in contrast to other fungi, the Oomycetes resemble higher organisms in being diploid in the vegetative state with meiosis occurring prior to gamete formation[1]. However, there is still little cytological information available for many important fungi in this group. Outstanding among these is the potato blight fungus, *Phytophthora infestans*.

We have made a cytological examination of the gametangia (antheridia and oogonia) of *P. infestans* formed on crossing isolate 63B (compatibility type A^1) with isolate 445 (A^2), and in cultures of 445 induced to self by the *Trichoderma* method[2]. These isolates have been widely used in earlier genetical work on this species[3-6].

In both types of material, crossed and selfed, two nuclear divisions normally occurred in the gametangia, and stages in meiotic prophase were observed. The chromosome number of *P. infestans*, from counts of first metaphase configurations, is 16–20 ($2(9 \pm 1)$).

Multiple associations of chromosomes were observed in some of the nuclei of the oogonia in both the paired and selfed material, and afford evidence that the divisions are indeed meiotic. The observation in several cases of an association of six chromosomes in the crossed material (Fig. 1) would seem to be evidence for structural hybridity rather than polyploidy. Thus one of the parents of the cross is believed to be a structural hybrid for a double interchange of chromosome parts involving three pairs of chromosomes, probably strictly analogous to that obtained in *Pisum sativum* and other higher plants when two single interchange lines are crossed[7]. Although selfed material of 445 was scanty, a multiple association was observed there also, so 445 must be a structural hybrid, possibly the parent with a double interchange. On data presently available it is not possible to determine the chromosome structure of 63B, although a more intensive investigation of 445 × 63B and of 63B in other combinations should provide evidence of its structure. The fact that antheridia attached to oogonia containing nuclei with multiple associations usually had uniform post-division nuclei may indicate that 63B is a structural homozygote.

The post-division stages of development were of considerable interest in both types of material. In the oogonia, while many periplasm nuclei were roughly half the size of the vegetative nuclei in nearby hyphae, suggesting a haploid condition in the former and a diploid in the latter, other nuclei of varying sizes were observed in the periplasm, indicating a failure of the second division in some cases. Sometimes giant "restitution" nuclei which could have resulted from the failure of both divisions were seen. In maturing oogonia two oospheres rather than the usual one were observed on several occasions. These observations suggest that more than one nucleus, reduced or unreduced, may be included in an oosphere. This could account for the genetical results of Laviola[4,5], who obtained more than one genotype among zoospore progenies of some single oospores from crosses in which isolate 445 was involved.

A high frequency of failure of oosphere formation or gametic abortion was observed in the crossed material. Similar high sterility has been reported in other crosses involving isolates 445 and 63B[5], and in crosses among F_1 progeny of 445 × 473[3]. This situation is possibly comparable to the situation in *Pisum sativum*, where 50% of pollen and ovule abortion occurs when an association of four chromosomes is present, and about 75% occurs when two associations of four or one of six are present. In a structural hybrid viable combinations are formed when every pairing segment segregates so that each daughter nucleus contains a balanced genetic complement. Other types of segregation lead to duplications of some segments and deficiences of others, and are therefore usually inviable. Unequal chromosome segregation leads to the formation of gametes with an extra chromosome and hence to the production of trisomics in the progeny.

In considering the sterility to be expected in *Phytophthora* three other factors must be taken into account. In the crossed material, oogonia and antheridia of both parents may be present and these may differ in chromosome structure. In such a case the percentage of oosphere abortion in a particular sample would depend upon the percentage of oogonia formed by each parent. Second, the oogonium is multinucleate, containing a number of nuclei undergoing meiosis. There is therefore a possibility that if one nucleus leads to inviable combinations another nucleus leading to viable combinations may provide a substitute nucleus for the oosphere. *Phytophthora* resembles higher animals rather than higher plants in that meiosis leads directly to gamete production without a gametophyte stage. Thus some deficient types may survive until fertilization when zygotic elimination may or may not occur

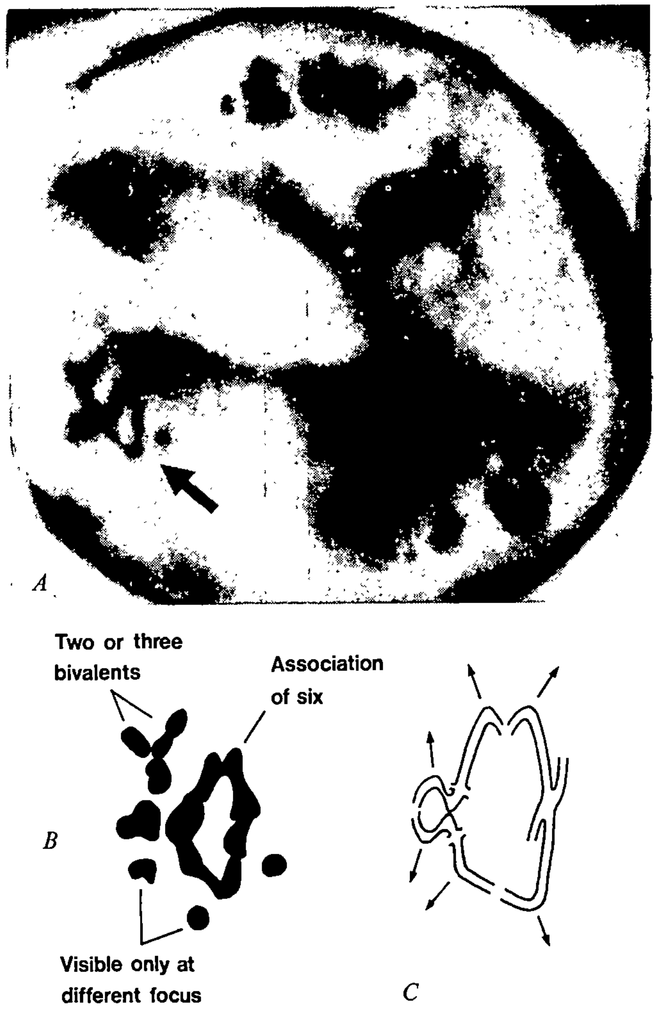

Fig. 1 *A*, Aceto-orcein squash of 445 × 63B (× *c*.13,000). An oogonium with a nucleus (arrowed) showing an association of six and four or five bivalents (two others out of focus). *B*, Drawing of the arrowed configuration. *C*, Possible interpret-ation of the association of six. Arrows indicate centromeres.

The nuclear behaviour in the material we have examined shows that meiosis occurs in the gametangia, indicating that *P. infestans*, in common with other Oomycetes[1], is diploid in the vegetative state. The occurrence of diploidy and structural hybridity in *P. infestans* should be of interest to those working on the genetics of pathogenicity and disease resistance in potato blight.

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Rediscovery of Fraser's Dolphin *Lagenodelphis hosei*

F. C. FRASER[1] described *Lagenodelphis hosei* in 1956 from a skeleton collected by E. Hose[2] before 1895 on a sea beach in Sarawak. There have been no further records of the species, and its external appearance has remained unknown. We report here the nearly simultaneous, very recent rediscovery of the species in three widely separated areas of the world, and describe its external coloration and form.

On January 27, 1971, at 5° N latitude, 95° 45′ W longitude (approximately 800 km west of Cocos Island in the eastern tropical Pacific), the catch of the seiner M/V Larry Roe included approximately twenty-five dolphins of a type unknown to the fishermen. A US National Marine Fisheries Service observer aboard photographed a large male (Fig. 1*a* and *b*) and collected a small calf (Fig. 1*c* and *d*) of these dolphins. On May 20, 1972, at 5° N latitude, 122° 22′ W longitude (about 2,560 km west of the 1971 locality), three more dolphins of the same type, all females, were captured in a net set on yellowfin tuna. The specimens, heavily damaged, have been acquired by the Museum of Comparative Zoology, Harvard University.

On February 17, 1971, at 30° 47′ S latitude, 30° 58′ E longitude (approximately 80 km south of Durban, South Africa), Best, Gambell, and Ross collected a pregnant female dolphin of an unfamiliar species (Fig. 1*e* and *f*). Two days later, at 30° 09′ S latitude, 32° 20′ E longitude an adult male of the same species (Fig. 1*g*) was collected. On February 17, 1972, another specimen, an immature female (Fig. 1*h* and *i*) was taken in the same area, at 29° 33′ S latitude, 32° 12′ E longitude.

On March 1, 1971, an adult female dolphin (Fig. 1*j* and *k*) of a species unfamiliar to local residents was washed ashore at Coffs Harbour, New South Wales, Australia (30° 10′ S latitude, 153° 10′ E longitude). D. H. Brown collected the specimen and forwarded it frozen to the University of Sydney.

We have compared the prepared skeletons of the 1971 South African specimens and the eastern Pacific calf with photographs and a partial cast of the type specimen of *L. hosei* and conclude that they belong to that species. The adult specimens (Table 1) agree closely with the type in meristics, measurements, and proportions (the two skulls bracket the type in over half of the proportional measurements), and the diagnostic features of the genus and species are clearly present (Fig. 2), namely, (generic characters) "general structure of skull including tympano-periotic bones as in *Lagenorhynchus* but rostrum having a pair of deep grooves on the palatal surface and fusion of the premaxillae in the middle line dorsally . . . in the manner of *Delphinus* but not of the same extent," and (specific characters) ". . . about 8 feet [2.5 m] long, with broad cranium and basal width of rostrum about 53% of rostrum length. Rostrum flattened, premaxillae not conspicuously raised above level of adjacent maxillae and not varying much in width throughout their rostral length. Post-temporal fossae of moderate size and suboval in shape. Teeth R 44/42 L 43/ca40. Lower jaw rami with a low rounded keel in the neighbourhood of the symphysis. Teeth length 13.6–17.3 mm, their greater diameter 3.9–4.6 mm and lesser 2.4–3.7 mm. Vertebral formula—cervical, 7; thoracic 15, lumbar 21; caudal 37—total number 80 (correct within one or two)."[1]

Agreement in meristics is well within the limits of individual variation to be expected on the basis of the range of variation for other, better-known delphinids. The premaxillae of the female specimen are not fused, but incipient fusion is indicated by convergence of the bones, as in young specimens of *Delphinus*. The calf agrees well with the type in meristics, the palate is grooved and the premaxillae converge. The skeletons of the eastern Pacific specimens collected in 1972, the Australian specimen and the third South African specimen have not yet been examined, but we refer them also to *L. hosei* on the basis of their close similarity with the other South African and the earlier eastern Pacific specimens in the distinctive colour pattern and in the external size and shape.

Fraser named his new genus *Lagenodelphis* because the skull of the type possesses features of the genera *Lagenorhynchus* and *Delphinus*. *L. hosei* is in some respects intermediate in external shape (Table 2) as well. The snout is short as in

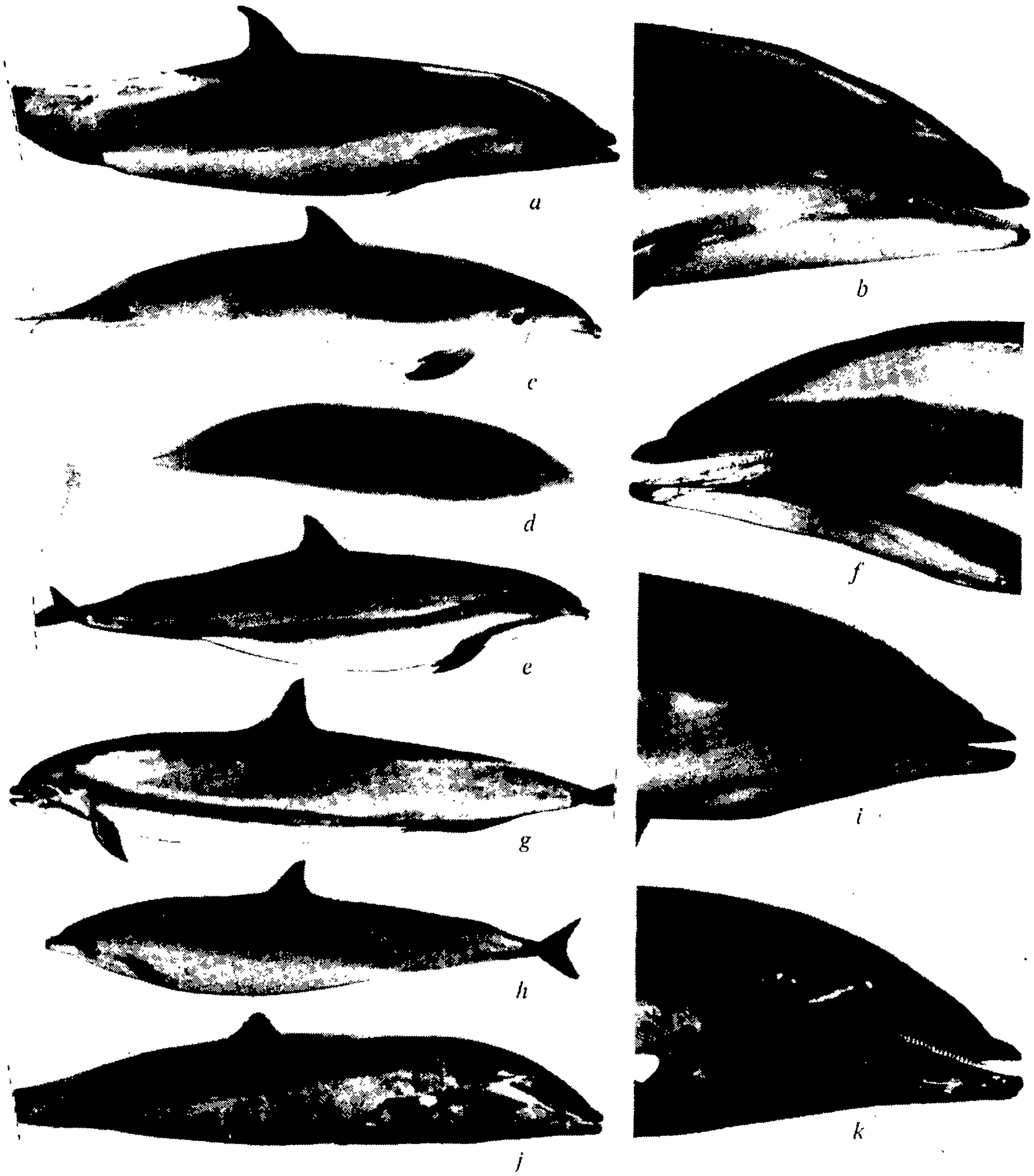

Fig. 1 *a* and *b*, Specimen LR22, male, 226 cm, from eastern Pacific. *c* and *d*, Specimen LR23, male, 110.2 cm, from eastern Pacific. *e* and *f*, Specimen PBB71/3 (SAM 36322), female, 236 cm, from off Natal, South Africa. *g*, Specimen PBB71/4 (SAM 36323), male, 264 cm, from off Natal, South Africa. *h* and *i*, Specimen PBB72/2 (PEM1517/93), female, 225.9 cm, from off Natal, South Africa. *j* and *k*, Specimen from off N.S.W., Australia, female, 226 cm.

Lagenorhynchus but well defined as in *Delphinus*. The overall build is relatively robust as in *Lagenorhynchus*, but the size and form of the appendages are as in *Delphinus*. The dorsal fin is only weakly falcate.

In a letter from Charles Hose to Sir Sidney Harmer dated October 23, 1923[1], the skin colour of the type specimen was described as "greyish or whitish yellow in parts, one might almost say cream colour, but a greyish brown in other parts.... The colour is difficult to describe, and it is more than twenty-five years ago." Hose's brother claimed that he had collected this specimen, and noted: "As far as I remember, it was not possible to recognize the colour of the skin, it was so very decomposed"[2]. The coloration of *Lagenodelphis* can therefore be considered as unknown. From colour transparencies of the new specimens, it can now be described as follows.

The most obvious feature is a single dark grey lateral stripe. The dorsum above the lateral stripe is dark greyish blue with a brownish hue, and the dorsal fin and both sides of the flippers and tail flukes are similarly coloured. There was a light patch in the centre of the dorsal fin of the large eastern Pacific specimen (Fig. 1*a*). The ventrum is white tinged with pink in the living and very recently killed animal. A typical delphinid bridle (terminology of Mitchell[3]) is present, with eye patch, eye stripe, blowhole stripe, and lip patch. There was a definite light grey-blue beak blaze in all animals except the calf, in which there was a suggestion of one. This blaze was bilaterally symmetrical, leaving a narrow strip of dark pigment in the midline of the beak. The blaze compresses the lip patch to a V-shaped patch at the tip of the snout and a narrow line around the edge of the gape, which connects with a similar V-shaped patch at the tip of the lower jaw.

The pattern may be considered in terms of interacting components, as has been done for other delphinids[4], as a basic "cape pattern" and a "dorsal field overlay". The ventral margin of the cape (best seen in the calf, Fig. 1*c* and *d*) arises at the apex of the melon, passes about 6 cm over the eye, dips ventrad to a low point about halfway between flipper base and dorsal fin, and then sweeps dorsad to an area between

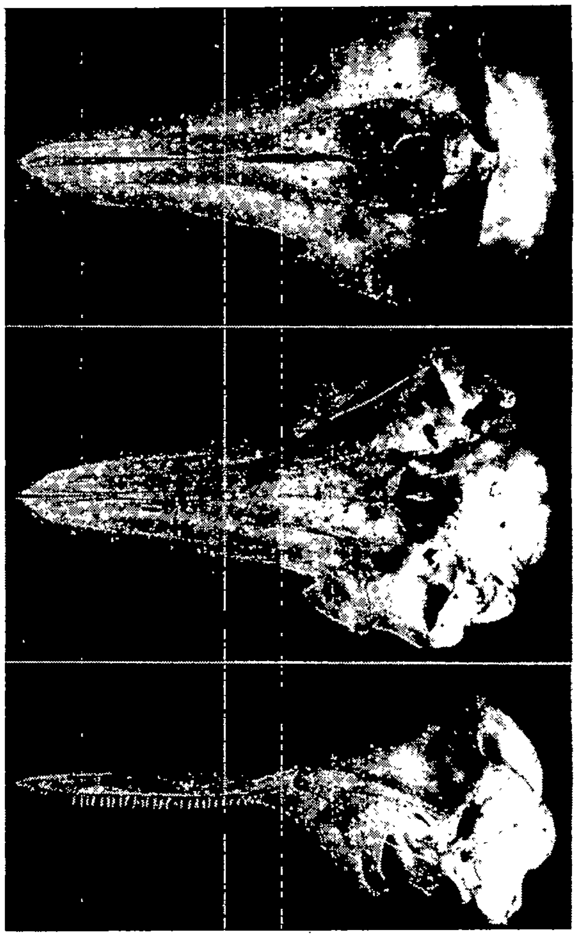

Fig. 2 Dorsal, ventral and lateral views of cranium of PBB71/4 (SAM 36323).

Table 1 Skeletal Measurements and Meristics of Four Specimens of *Lagenodelphis hosei* Fraser, 1956, including the Holotype

Measurement or count	Sarawak specimen (holotype, BMNH1895.5.9.1)* physically mature (from Fraser, 1956)	South African female PBB71/3 (SAM ‡ 36322), physically mature	South African male PBB71/4 (SAM ‡ 36323), physically mature	Eastern Pacific calf LR23 (USNM † 396079)
Condylobasal length	413 mm (100%)	429	440	
Length of rostrum	226 (54.7)	240 (55.9)	241 (54.8)	
Width of rostrum at base	121 (28.3) (53.5% of rost. ln.)	119 (27.7) (49.6% of rost. ln.)	130 (29.5) (53.9% of rost. ln.)	
Width of rostrum at midlength	71 (17.2)	71 (16.6)	80 (18.2)	
Width of rostrum 60 mm anterior to antorbital notches	85 (20.5)	86 (20.0)	101 (23.0)	
Least supraorbital width	202 (48.8)	202 (47.1)	218 (49.5)	
Preorbital width	207 (50.1)	207 (48.3)	223 (50.7)	
Postorbital width	230 (55.7)	229 (53.4)	247 (56.1)	
Zygomatic width	225 (54.5)	225 (52.4)	240 (54.5)	
Parietal width	170 (41.2)	161 (37.5)	177 (40.2)	
Maximum width of premaxillae	82 (19.9)	78 (18.2)	83 (18.9)	
Length of upper left tooth row	194 (46.9)	193 (45.0)	213 (48.4)	
Length of lower left tooth row	193 (46.7)	198 (46.2)	207 (47.0)	
Length of left ramus	350 (84.7)	367 (85.5)	375 (85.2)	
Coronoid height of left ramus	70 (16.9)	65 (15.2)	71 (16.1)	
Length of symphysis	36 (8.7)	37 (8.6)	31 (7.0)	
Number of teeth	$\frac{43 \mid 44}{\textit{ca. } 40 \mid 42}$	$\frac{40 \mid 42}{39 \mid 39}$	$\frac{42 \mid 42}{41 \mid 40}$	$\frac{42 \mid 42}{42 \mid 44}$
Total number of vertebrae	80±2	78	78±1	79
Vertebral formula	C7T15L21C37±2	C7T16L21C34	C7T16L+C55±1¶	C7T16L+C56§

* British Museum (Natural History), London.
† US National Museum, Washington, DC.
‡ South African Museum, Cape Town, SA.
§ Counts from radiographs of carcass.
¶ Vertical column disarticulated during preparation; 1–3 small terminal vertebrae missing.
Percentage of condylobasal length in parentheses.

dorsal fin and flukes, where it fragments into a series of diagonal lighter brushings that impart to the posterior half of the animal a chevron pattern when seen from above. The distinctive lateral stripe (eye-to-anus stripe in terminology of Mitchell[3]) is subsidiary and subparallel to the cape. It also arises at the apex and closely parallels the cape margin for about half the length of the body, diverging ventrad behind the dorsal fin and becoming diffuse above and behind the genital region.

The stripe varies markedly among the specimens in width, clearly defined length, and intensity of pigmentation, in apparent correlation with age. In the calf (Fig. 1*c*) and the subadult female (Fig. 1*h*) it is relatively narrow, passing above the eye, and becomes obscure before reaching the genital region. In the larger male from the eastern Pacific (Fig. 1*a*) (of unknown degree of maturity), the stripe is broader, encompassing the dorsal half of the eye, and is well defined for its entire length to where it interacts with the dorsal overlay system (discussed below) in the genital region. La Grange noted "considerable variation" in the intensity and definition of the stripe among the animals captured with this specimen, some having broader and darker stripes. Observations of animals at sea off the Natal Coast of South Africa indicated that pigmentation of this area was related to size of the animal. In the adult male and female from South Africa (Fig. 1*e–g*) both larger than the eastern Pacific male, the stripe is still broader, encompassing the eye completely. It appears to be broader than it actually is, however, as its ventral margin can be discerned upon close examination but is obscured by heavy pigmentation of the ventral portion of the dorsal field overlay. In the smaller specimens these two elements are distinct one from the other.

The dorsal field overlay encompasses the flipper stripe and overlaps completely the cape and eye-to-anus stripe. This feature also shows graded development correlated with size, being more lightly pigmented in the smaller specimens. There is a narrow but well-defined light line of demarcation between the anterior end of the flipper stripe and the lip patch. The flipper stripe has a double structure, which is the more clearly defined in the younger animals. The dorsal field in all the specimens has one or two thin posteriorly directed extensions that diverge from the ventral margin and run parallel for several centimetres before disappearing or rejoining the field.

In the genital region of the large eastern Pacific male (Fig. 1*a*), some interaction can be seen between the eye-to-anus stripe and the structure of the dorsal field overlay. Similar interactions between colour pattern elements may be observed in species of *Lagenorhynchus*[3]. In the South African adults the interaction is obscured by heavier pigmentation of the dorsal field in this region. Although indications strongly suggest that this and the other trends discussed above are related to development, an alternative explanation of geographical variation cannot be eliminated until known adult specimens from the eastern Pacific and other areas are compared to the South African adults.

Not seen in any of the specimens so far collected, but observed in animals at sea off the Natal coast of South Africa, is a spinal blaze (terminology of Mitchell[3]) extending from the light-coloured part of the side in a curve up towards the insertion of the dorsal fin.

Similarities in coloration of *Lagenodelphis* to any of the *Lagenorhynchus* species are difficult to demonstrate; there is no tendency towards development of a flank blaze so char-

Table 2 External Measurements of Six Specimens of *Lagenodelphis hosei* Fraser, 1956

	Eastern Pacific specimens		South African specimens			Australian specimen
Measurement or count	LR22, male, unknown degree of maturity	LR23 (USNM* 396079), male calf, 19.3 kg	PBB71/3 (SAM† 36322) adult female, 164 kg	PBB71/4 (SAM† 36323), adult male, 209 kg	PBB72/2 (PEM‡ 1517/93), subadult female 130 kg§	———, adult female
Total length	226 cm (100%)	110.2	236	264	225.9	226
Tip of upper jaw to centre of eye	—	17.7 (16.1)	33 (14.0)	33 (12.5)	33.1 (14.7)	29.5 (13.1)
Tip of upper jaw to apex of melon	4.5 (2.0)	1.8 (1.6)	4.5 (1.9)	3 (1.1)	4.8 (2.1)	3.5 (1.5)
Length of gape	—	14.3 (13.0)	27.5 (11.7)	27 (10.2)	28.0 (12.4)	24 (10.6)
Tip of upper jaw to external auditory meatus	—	21.1 (19.1)	—	39 (14.8)	38.2 (16.9)	34.5 (15.3)
Centre of eye to angle of gape	—	4.0 (3.6)	5.5 (2.3)	6 (2.3)	6.0 (2.7)	4.4 (1.9)
Centre of eye to centre of blowhole	—	11.0 (10.0)	21 (8.9)	23 (8.7)	19.7 (8.7	17.6 (7.8)
Tip of upper jaw to blowhole	—	16.5 (15.0)	33.5 (14.2)	28 (10.6)	30.9 (13.7)	28.6 (12.7)
Tip of upper jaw to anterior insertion of flipper	—	24.5 (22.2)	46 (19.5)	43 (16.3)	45.8 (20.3)	42.0 (18.6)
Tip of upper jaw to tip of dorsal fin	—	61.0 (55.4)	133 (56.4)	132 (50.0)	118.4 (52.4)	—
Tip of upper jaw to umbilicus	—	51.5 (46.7)	110 (46.6)	116 (43.9)	106.9 (47.3)	—
Tip of upper jaw to centre of genital aperture	—	71.3 (64.7)	165 (69.9)	170 (64.4)	157.2 (69.6)	—
Tip of upper jaw to centre of anus	—	78.8 (71.5)	175 (74.2)	189 (71.6)	187.7 (83.0)	—
Projection of lower jaw beyond upper	—	0	0.3	1	0.6	0.4
Girth at axilla	—	61.7 (56.0)	110 (46.6)	—	106.9 (47.3)	—
Maximum girth	—	—	132 (55.9)	—	116.5 (51.6)	—
Girth at anus	—	37.9 (34.4)	70 (29.7)	92 (34.8)	70.0 (31.0)	—
Width of blowhole	—	2.0	2.5	4	2.5	2.4
Length of flipper, to anterior insertion	25.1¶ (11.1)	15.2 (13.8)	27 (11.4)	28.8 (10.9)	26.7 (11.8)	25.5‖ (11.3)
Length of flipper, to axilla	18.8¶ (8.3)	10.5 (9.3)	19.5 (8.3)	21.5 (8.1)	20.0 (8.9)	17.3‖ (7.7)
Width of flipper	6.6¶ (2.9)	4.8 (4.4)	8 (3.4)	9.4 (3.6)	8.3 (3.7)	8.1‖ (3.6)
Height of dorsal fin	17.8¶ (7.9)	7.6 (6.9)	17 (7.2)	22 (8.3)	15.9 (7.0)	15.0‖ (6.6)
Span of flukes, tip to tip	49.5¶ (21.9)	22.8 (20.7)	57 (24.1)	59 (22.3)	50.9 (22.5)	47.0‖ (20.8)
Width of fluke, from notch to nearest point on anterior border	—	7.7 (7.0)	13 (5.5)	14.2 (5.4)	13.4 (5.9)	12.6‖ (5.6)

Percentage of total length in parentheses. Measurements taken as specified by Committee on Marine Mammals, American Society of Mammalogists[6].

* US National Museum, Washington, DC.

† South African Museum, Cape Town, SA.

‡ Port Elizabeth Museum, Port Elizabeth, SA.

§ Measurements converted from inches and eighths to centimetres and tenths.

¶ Measured 10 h after death; some dehydration probable.

‖ Measured after exposure to Sun; some dehydration probable.

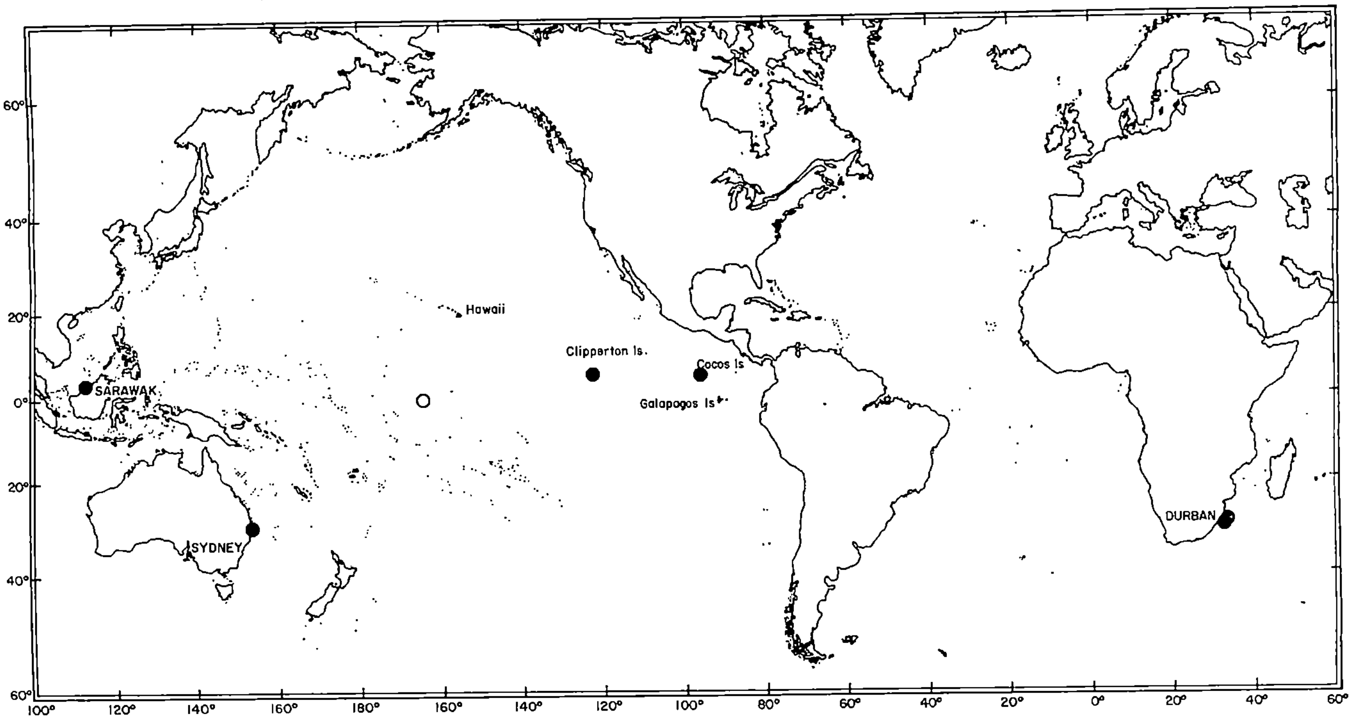

Fig. 3 Recorded occurrences of *Lagenodelphis hosei*. White circle represents sighting record.

acteristic of that genus[3], aside from the above-discussed propensity to posterior interaction of the eye-to-anus stripe and dorsal field. The species seems much closer to the *Stenella-Delphinus* group. The overall colour pattern of the adult *Lagenodelphis* is very similar to that of *Stenella coeruleoalba* with the exception of the flipper stripe, which in *S. coeruleoalba* runs to the eye or angle of gape[5], and the lack of a subtending line below the eye-to-anus stripe in *Lagenodelphis*. A comparison of the young *Lagenodelphis* with *Delphinus* reveals several features in common to both, especially if the longer beak of the latter is taken into consideration. The arrangement of the flipper stripe and eye-to-anus stripe is very similar in both species. The longer mandible of *Delphinus* seems to affect the relative position of these features, so that the flipper stripe extends farther forward in *Delphinus*, and the eye-to-anus stripe is correspondingly farther forward in the head region than in *Lagenodelphis*. *Delphinus* differs markedly, of course, in the development of a large, brightly-coloured thoracic patch (terminology of Mitchell[3]) which results from the unique partial overlap of cape and dorsal field and which is completely absent in *Lagenodelphis*.

The widely separated localities of collection reported here (Fig. 3) and the close similarity of the specimens to each other suggest that the species may be continuously distributed in high-seas tropical waters of the Pacific and Indian Oceans. It has also probably been sighted in the Central Pacific. On August 11, 1966, Balcomb observed a school of approximately four hundred dolphins at 165° W longitude on the equator (northeast of the Phoenix Islands). A field sketch and photographs (Fig. 4) clearly show the short, well-defined snout, small subfalcate dorsal fin, small flippers, chunky build, and distinct lateral dark stripe of *L. hosei*.

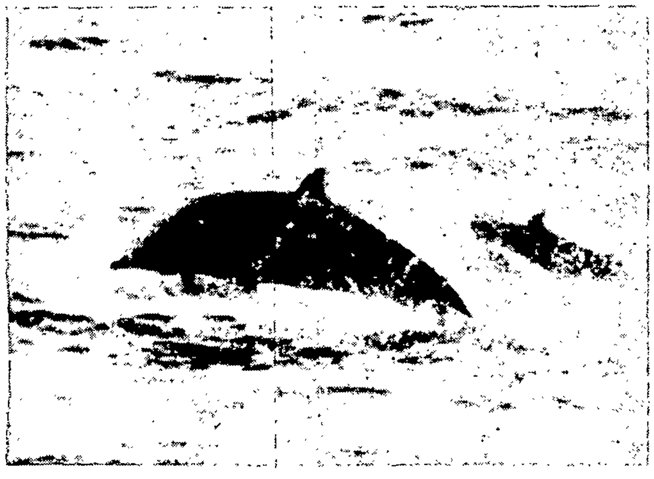

Fig. 4 Photo of dolphin sighted by Balcomb northeast of Phoenix Islands.

We thank John La Grange for collecting the eastern Pacific calf and bringing it to our attention, Captains J. Luz of the seiner Larry Roe and J. Adams of the Concho for their assistance, and James G. Mead for preparing the skull of the specimen and providing radiographs of the carcass of the calf. Captain T. Haakestadt and the crew of the whale-catcher C. G. Hovelmeier gave much valuable help in the collection of the South African specimens. We also thank David H. Brown for bringing the Coffs Harbour specimen to our attention. William E. Schevill very kindly allowed us to include the 1972 eastern Pacific record. Edward D. Mitchell provided excellent photographs of the holotype. Kenneth S. Norris, Carl L. Hubbs, and Dale W. Rice read the manuscript.

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The Influence of Prehistoric Cultures upon the Initiation and Spread of Blanket Bog in Upland Wales

THE shallow blanket peats of northern and western parts of the British Isles have received relatively little attention from palynologists. Conway's early work[1] on the Pennines was mainly concerned with deep peats accumulating in high altitude basins and plateaux (for example Ringinglow) which began forming during the Atlantic period. Pollen diagrams of shallower peats on sloping ground from a variety of areas (such as the Pennines[2], the Lake District[3] and Central Wales[4,5]) suggest their formation began at a rather later date, often about the time of the elm decline.

These shallow peats frequently contain wood remains in their basal layers which give way to an acidic bog peat of *Eriophorum* and *Sphagnum*[5]. Even where wood is absent, there is often evidence from pollen in the underlying soil that there was a former tree cover[6]. The spread of these upland peat bogs and consequent demise of former woodlands has usually been considered due to deteriorating climate, especially a rising precipitation/evaporation ratio. Here I postulate that this vegetational regression was hastened by early human activity of woodland clearance and more especially by stock grazing. This hypothesis is supported by pollen data from a shallow peat near Barmouth in Merioneth, Wales.

Fig. 1 shows the location of the sampling site, close to Llyn Irddyn at 1,000 foot altitude in the Dyffryn Ardudwy coastal region of Merionethshire, Wales (NGR: SH 628222). This area was chosen because of the local concentration of megalithic tombs shown in Fig. 1, and the inset gives the geographical distribution of Neolithic remains in Wales (drawn from the data of Grimes[7]). The megalithic structures of the Ardudwy region are of the distinctive western long cairn type[8,9] found in the Lleyn and Pembroke peninsulas of Wales, in Ireland and in Western Scotland.

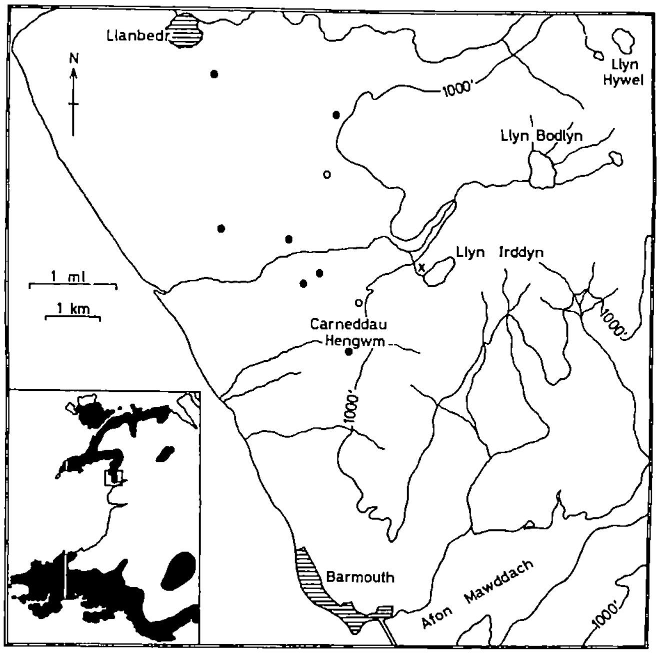

Fig. 1 Map of Barmouth area, Merioneth. ●, Megalithic tomb; ○, stone circle; ×, sampling site. Inset, Wales showing areas with Neolithic remains.

The site was the closest peat deposit of more than 30 cm depth to the Carneddau Hengwm complex of burial chambers, and it is given that name. Table 1 shows the peat stratigraphic profile. It thus provides an opportunity to study the ecological processes which were operative during the transition from upland wet alder wood to blanket bog. The basal wood peat and the transitional part of the stratigraphy were subjected to pollen analysis using contiguous 0.5 cm samples taken from a peat monolith collected in the field. Results of these analyses are shown in Figs. 2 to 6.

All data (except for fern spores) are expressed as a percentage of the arboreal pollen sum (excluding *Corylus* and *Salix*); 150 tree pollen grains were counted in each sample.

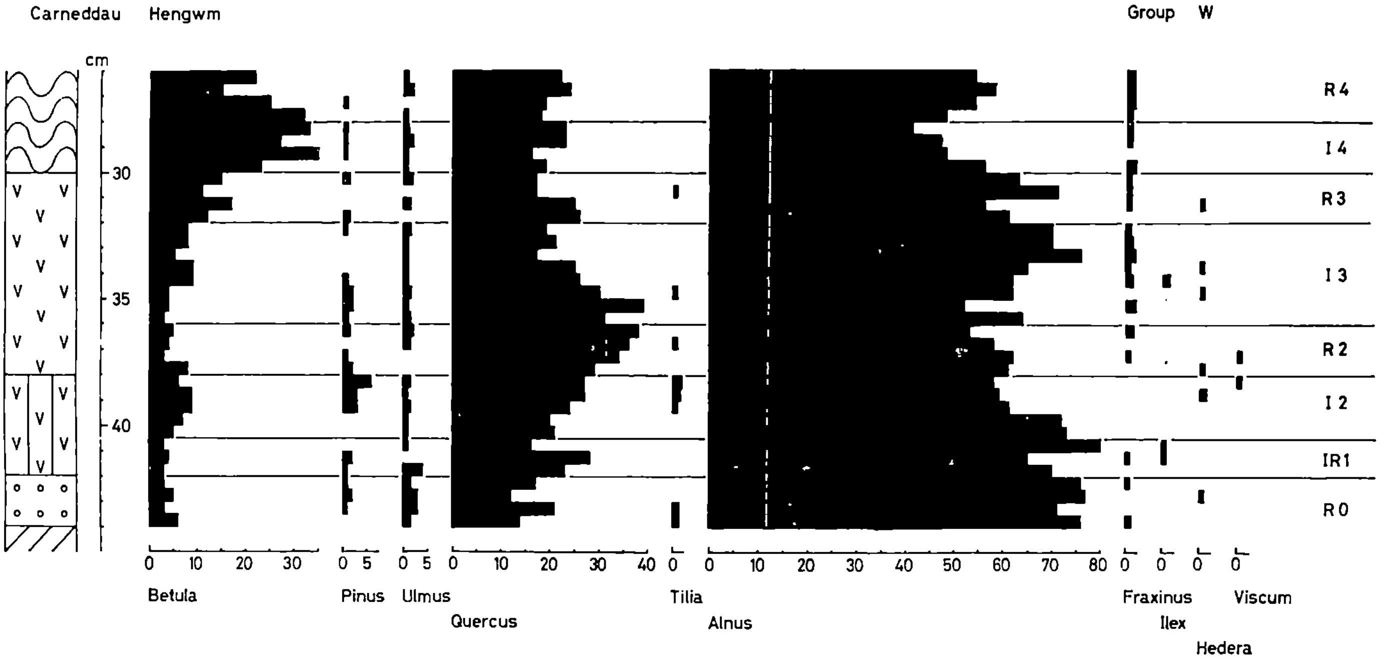

Fig. 2 Stratigraphic profile of the Carneddau Hengwm site and pollen diagram of Group W types, expressed as percentage arboreal pollen. Wavy lines, *Sphagnum* peat; V shading, wood peat; vertical lines, fen peat; circles, downwash gravel.

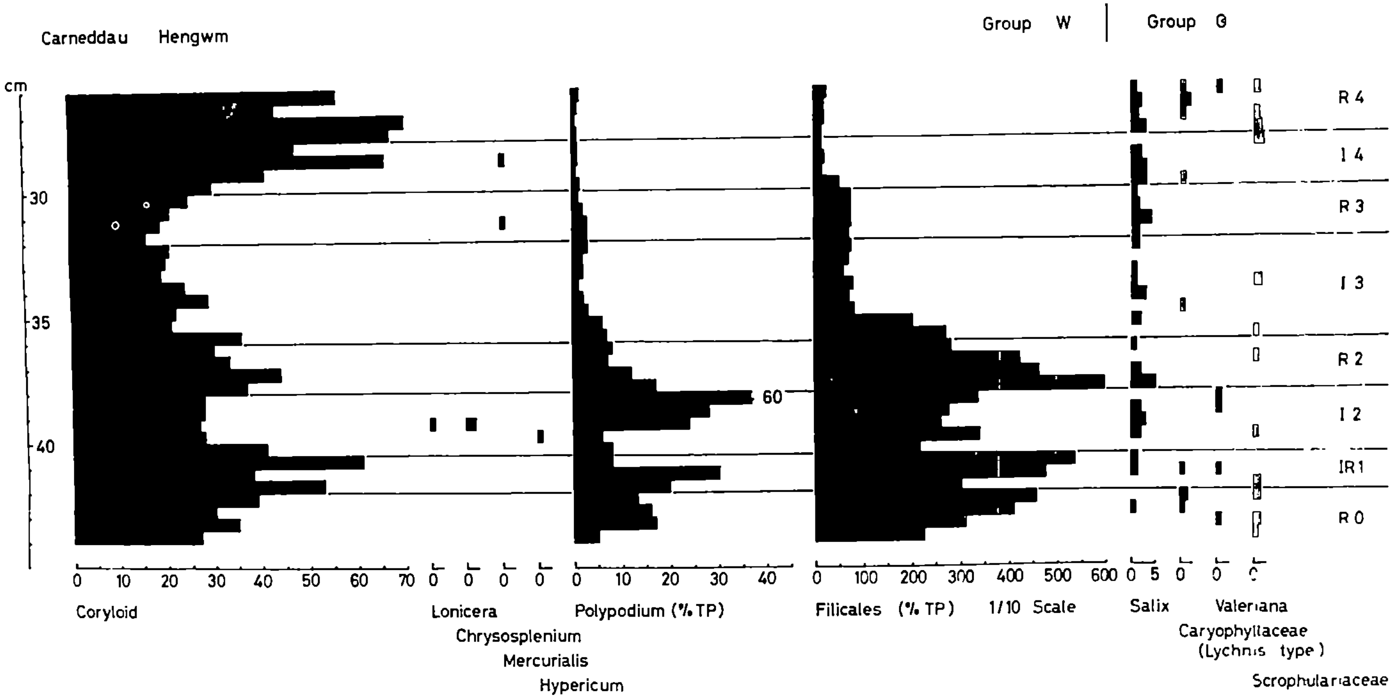

Fig. 3 Pollen diagram of Group W (continued) and Group O types.

Table 1 Stratigraphic Details of the Peat Profile; Macroscopic Remains in Peat

Depth	
0–23 cm	Bog peat of *Sphagnum*, *Eriophorum* and *Juncus*
23–30 cm	*Sphagnum* bog peat with some seeds indicative of more eutrophic conditions, for example, *Juncus bufonius* and *Lychnis flos-cuculi*
30–38 cm	Alder (*Alnus*) wood peat with *Juncus*, *Carex* and *Lychnis* seeds
38–42 cm	Highly decayed alder wood with fungal (*Cenococcum*) fruiting bodies
42–44 cm	Gravel and silt with *Juncus effusus* seeds

The dominance of *Alnus* pollen was not sufficiently great to necessitate its exclusion from the tree pollen sum[10] and expression of local pollen types using a local pollen sum basis[11] was not considered helpful here.

In the pollen diagrams the pollen types have been divided into seven groups on the basis of their ecological requirements (Table 2). Some overlap is inevitable where pollen types such as Gramineae may be represented in more than one group. The diagram has been zoned on its inherent features, especially those which may relate to disturbance of woodland by humans or their animals ('I' phases) and those features associated with recovery and regeneration following such

Table 2 Key to the Habitat Groupings of Species in the Pollen Diagrams

(W) Woodland, including species of wet woodland floors which might also belong to group O (for example, *Chrysosplenium*).
(O) Open woodland.
(B) Poor pasture and blanket bog.
(H) Aquatic habitats.
(P) Grassland and habitats managed for pastoral agriculture.
(F) Arable land.
(A) Montane habitats.

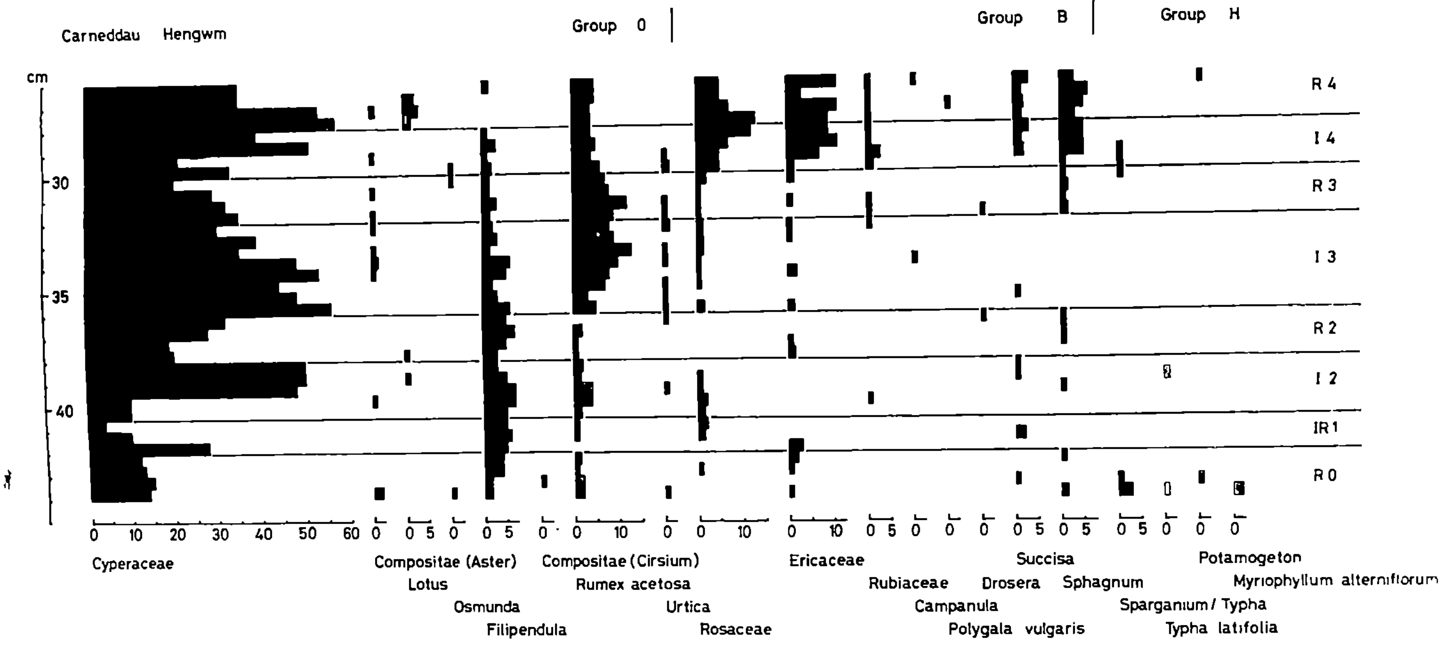

Fig. 4 Pollen diagram of Group O (continued), Group B and Group H types.

Table 3 Description of the Pollen Zones and their Interpretation

Pollen zone	Features	Possible causes
R0	Peat initiation, increasing ferns and *Filipendula*	Little human activity. Canopy may have been opening as woodland became wetter
IR1	Fall in *Alnus* ; rise in *Quercus*, fern spores and *Juniperus* pollen	Local clearance opening the canopy and allowing a greater proportion of regional pollen into the peat. Regeneration follows
I2	Increase in herbaceous, marsh species. *Plantago lanceolata* appears in quantity	Local and regional clearance. Pastoral and arable activity on a regional scale; possible local eutrophication
R2	Increase in *Alnus*, and in species of group B	Canopy closure; reduced local diversity; local and regional regeneration
I3	*Filipendula* and ferns decrease; *Urtica* and *Rumex acetosa* increase, *Quercus* decreases, *Betula* and *Fraxinus* increase, cereal pollen appears	Major regional interference phase with arable cultivation. Local flora shows trend towards low nutrient status with the exception of *Urtica* which may indicate local phosphate flushing
R3	*Rumex acetosa* and Cyperaceae fall; bog types increase; *Juniperus* reaches a peak; seed of *Juncus bufonius* in stratigraphy	Some regional regeneration. Locally grazing and trampling may have continued
I4	*Alnus* falls and *Betula* increases; increases in Gramineae, *Plantago*, *Pteridium* and bog types	Considerable local changes, the *Alnus* woodland degenerating to open bog. Regional changes difficult to discern because of major local changes, but failure of *Quercus* to rise as *Alnus* falls suggests concurrent regional woodland clearance
R4	High Cyperaceae, probably *Eriophorum* (see stratigraphy), some recovery of *Quercus* and *Alnus*	Continued bog development locally. Some woodland regeneration on a regional scale

interference ('R' phases), see Table 3. Some of the local and regional changes in vegetation have resulted in changes in the overall diversity as well as the specific composition of the pollen rain. Diversity here is represented by Shannon's diversity index[12,13] which is given by the formula

$$D = -\Sigma\ p_i\ l_n\ p_i$$

where p_i is the number of grains of the *i*th species divided by total grains. The index will be minimal where all grains are of a single species and maximal where each species is represented by only one grain.

Diversity at each level was computed for both total data and for the local elements on their own. Total diversity (Fig. 6) increases in steps up the profile. There are two possible explanations for this: (i) local vegetation is becoming more diverse, or (ii) the opening of the canopy allows a more diverse pollen representation. Generally there is a tendency for total diversity to increase rapidly during interference phases and to fall, or remain steady, during regeneration phases.

Local diversity is difficult to ascertain because one cannot determine accurately the proportion of pollen input which can be considered local. The local flora in the basal wood peat and the upper bog peat were different, so the basis for determining local types changes at a depth of 30 cm. Below 30 cm the local diversity curve follows the pattern of total diversity very closely, being greatest during the interference phases and showing a general increasing trend. Above 30 cm the curve becomes erratic, but is on average lower than in phases I3 and R3.

Evidence from the site suggests that, during the period of peat initiation, humans were active in this area, and that their activities had a progressively deleterious effect upon both the local and the regional vegetation. The change in local pollen, both in diversity and specific composition, during interference phases is of particular interest. It demonstrates how human activity, such as shrub or canopy clearance, firing or stock grazing, could have accelerated the degeneration of a damp woodland ecosystem and assisted the spread of blanket bog.

The immediate effects of human activity appear to have been short-term environmental perturbations which have

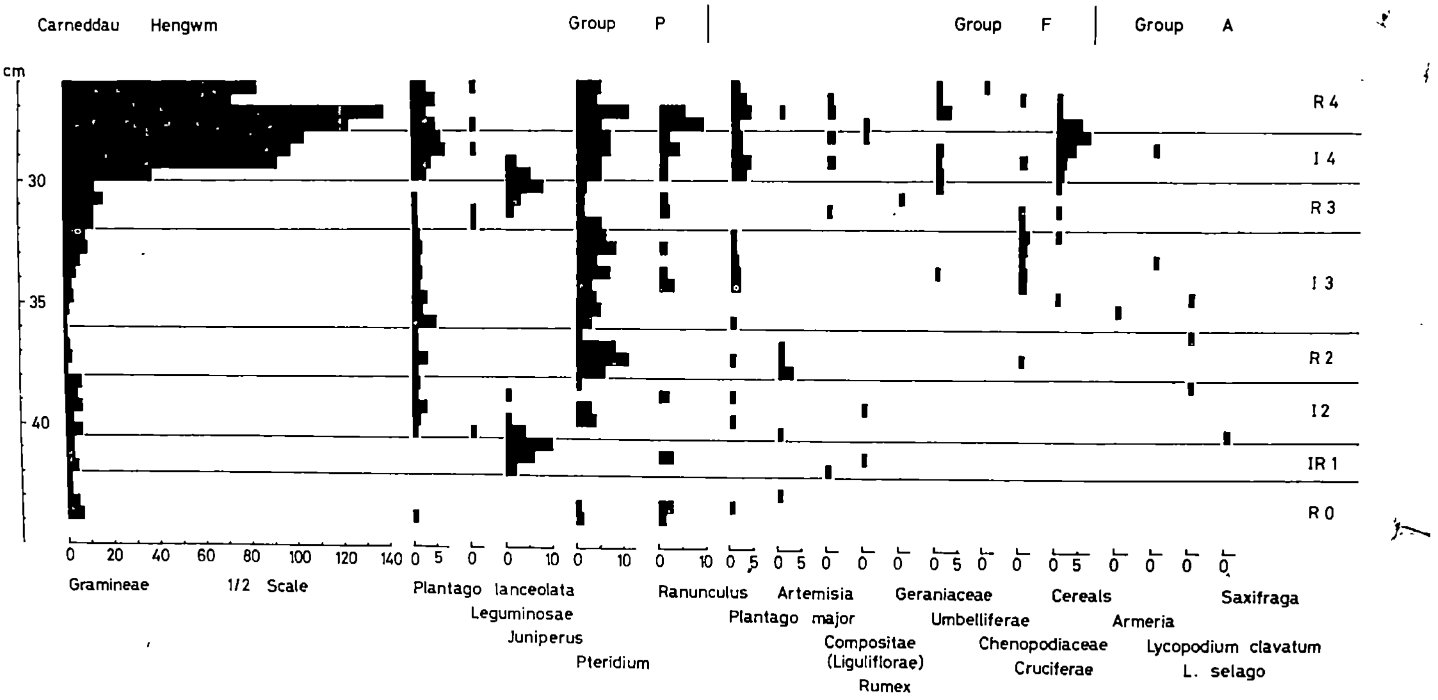

Fig. 5 Pollen diagram of Group P, Group F and Group A types.

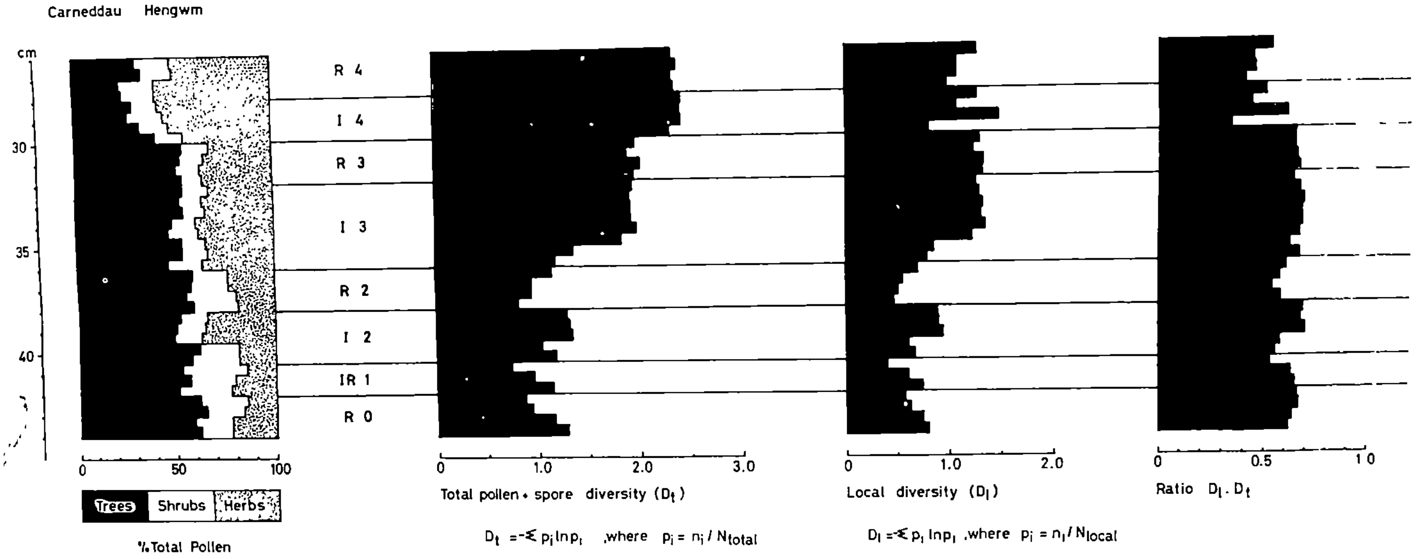

Fig. 6 Summary pollen diagram and pollen and spore diversity diagrams.

increased floral diversity by opening the canopy and eutrophicating the system. Some plants, such as *Juncus bufonius*, may even have been brought in by movements of grazing animals. Continued repetition of such disturbance in a climatic regime where liberated nutrients were subject to leaching inevitably led to retrogressive developments in the ecosystem similar to those described by Iversen at Draved, Denmark[14]. The degeneration occurred in a series of steps, being accelerated at each interference phase. The final step led to the collapse of woodland and the initiation of blanket bog.

Thus at Carneddau Hengwm the retrogressive processes described appear to be a consequence not only of a deteriorating climate, which would assist in soil leaching, but also of a series of interferences with upland woods by man and his grazing animals, perhaps commencing in Neolithic times. This must have contributed to the spread of blanket bog in the area.

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Action of Black Widow Spider Venom on an Aminergic Synapse

AT the frog neuromuscular synapse Black Widow Spider venom (BWSV) transiently increases the frequency of the spontaneous miniature end-plate potentials before abolishing the miniature discharge[1], these changes being accompanied by depletion of the synaptic vesicles in the terminals of the motoneurones[2]. It has been suggested that the action of this venom is restricted to cholinergic systems[3], a suggestion possibly supported by its inactivity at the squid giant synapse (R. Miledi, personal communication). The fact that studies using fluorescence histochemical techniques indicate that BWSV also depletes transmitter at catecholamine synapses[4] seems, however, to refute this. In view of this it seemed worth while to examine the effect of BWSV on a non-cholinergic synapse, the insect nerve-muscle synapse where transmission is glutamatergic[5]. The results of these studies were quite unequivocal; BWSV has qualitatively similar effects on glutamate and acetylcholine synapses.

Desiccated whole poison apparati (Sigma grade II) were ground up in locust saline[6] and applied to metathoracic extensor tibiae[7] and retractor unguis[9] muscle fibres of the locust *Schistocerca gregaria*. The BWSV did not significantly alter the osmolarity and *p*H of the saline. In most experiments 5 apparati per 10 ml. were used but, because of their low and variable activity, toxicity could not be standardized. After a variable delay (10–60 min) the miniature discharge of these muscle fibres became very irregular, periods of high frequency (> 100 miniature potentials/s) (Fig. 1) being separated by periods of near normal frequency (≃ 3 miniature potentials/s). The cyclic nature of these changes may be due to the complex multiterminal innervation of insect muscle fibres[9], the venom acting with a variable delay and to a variable extent at different synaptic sites. Similar results were obtained with venom in saline containing sufficient magnesium (50 mmol/l.) to completely block impulse-linked release of transmitter. Miniature potentials could still be recorded from some fibres 12 h post venom treatment although the pattern of the miniature discharge was irregular and the miniature potentials occurred at a very low frequency (1/5 s) (Fig. 2).

A number of nerve-muscle preparations perfused for 4 h with BWSV were fixed with 4% glutaraldehyde and phosphate buffers for 2 h and then post-fixed with 1% OsO_4 for 1 h. Some axon terminals were almost devoid of synaptic vesicles, others contained clumps of vesicles adjacent to the presynaptic membrane[9], whilst the rest appeared quite normal (Fig. 2). Depleted terminals contained membrane bound structures similar to those seen in lanthanum treated nerve terminals in frog muscle[10]. It appears from these data that changes in number and distribution of synaptic vesicles in terminals of insect motoneurones treated with BWSV correlate well with

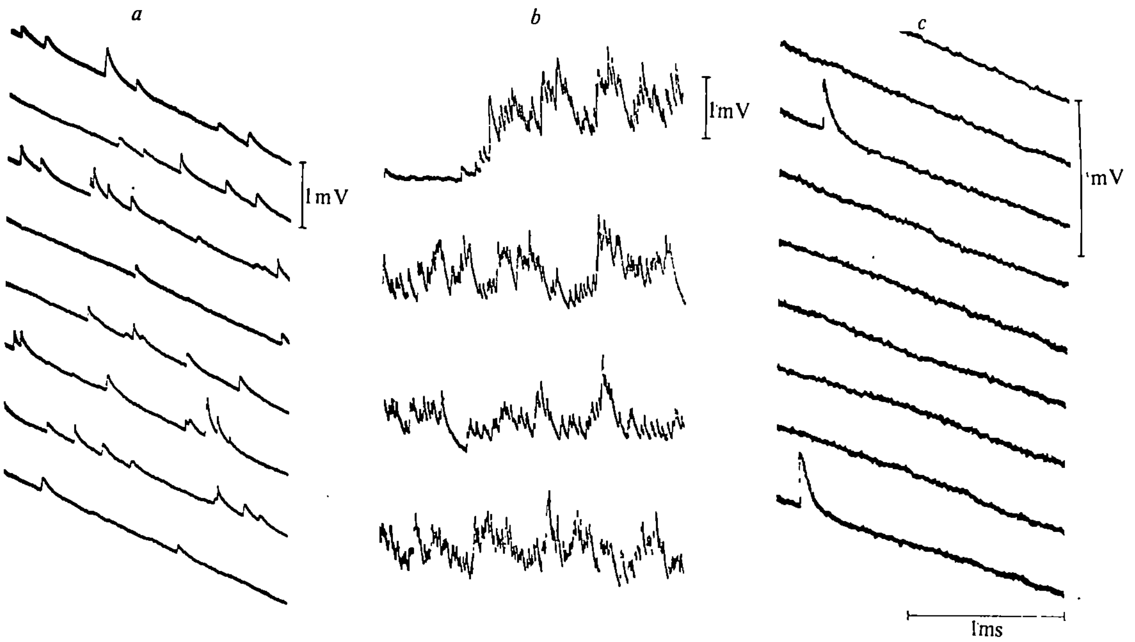

Fig. 1 Miniature discharges recorded from a locust extensor tibiae muscle fibre. *a*, Before treatment with Black Widow Spider venom (BWSV). *b*, During the onset of BWSV action. *c*, 12 h after BWSV treatment.

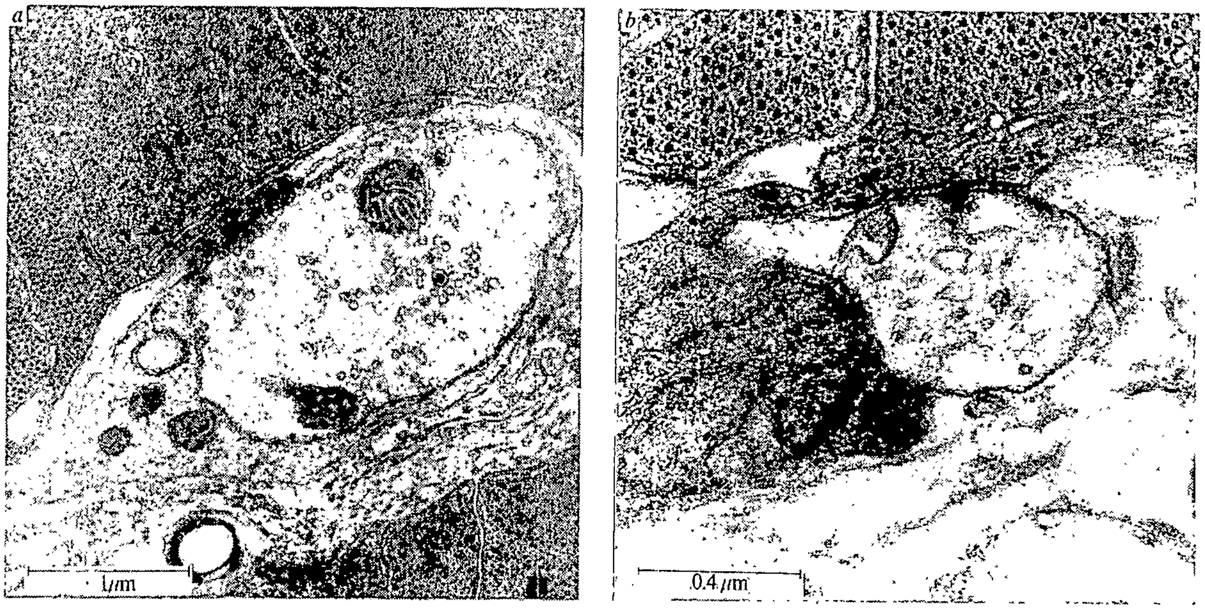

Fig. 2 *a*, Electron micrograph of a normal locust nerve-muscle synapse containing synaptic vesicles. *b*, Electron micrograph of a locust nerve-muscle synapse after treatment with Black Widow Spider venom showing paucity of synaptic vesicles and presence of numerous irregularly-shaped membrane bound structures.

changes in the spontaneous release of transmitter from these terminals.

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Corrigendum

THE authors are indebted to Mr J. Serene for pointing out an error in the derivation of the frequency shift in the article "Properties of a Possible Superfluid State of ^{3}He" by P. W. Anderson and C. M. Varma (*Nature*, **241**, 187; 1972). As the calculation is stated, the quantity d in equation (9) is unitary and commutes with Δ, and thus gives no splitting of the states of different spin. The fact that we obtain essentially the correct quantitative answers is, however, not a coincidence; a correct derivation which is mathematically similar but based on different principles has been discovered and will be published shortly.

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What Future for British Broadcasting ?

SIR JOHN EDEN, the Minister for Posts and Telecommunications, must announce soon whether or not the government will set up an inquiry into the future of broadcasting. Time is getting short. The charter of the British Broadcasting Corporation and the licence of the Independent Broadcasting Authority expire in mid-1976. The licences for the companies like Rediffusion and British Relay which sell cable or wired television service also run out at the same time and so does the contract between the BBC and the Open University. Already the IBA is in the awkward position of preparing to award franchises for commercial radio stations which could—depending on when the three-year radio licences actually begin—extend beyond the limits of the IBA's statutory life. The usual length of the television authorities' franchises has been 12 years. So whatever decisions are taken by Parliament about broadcasting in the next year or two could fix the shape of Britain's television until 1988.

The report the government was ostensibly waiting for (see *Nature*, **241**, 1 ; 1973) was delivered to Parliament a year late, in December. It was slipped in after questions on the Wednesday before Christmas, and the pressure is on Sir John to say what will happen next. But it is a good guess that the delay means that there is to be no formal inquiry at all. The strongest rumour so far is that the government will submit legislation extending the franchises of the BBC and the ITA until 1981.

There are other possibilities. The government is having to take into its calculations the fact that there must be a general election before June 1975. If it were to extend the lives of the BBC and the ITA for one extra year, until mid-1977, then there would be time for a full committee of inquiry to be set up now and continuing working uninterrupted (provided the Conservatives won again) through the election tension, preparing the recommendations about the long-term future of broadcasting. Or the government might appoint a small committee, a few wise men, to study the subject without hearing the usual vast array of witnesses, and then go ahead with its legislative proposals.

It does seem unlikely that the government would undertake to set the course of broadcasting for a dozen or more years without giving an airing to the many groups who hold passionate and conflicting views about how television should be organized. Several groups have already decided to go ahead on their own. The Social Morality Council has a committee, under the chairmanship of Dame Margaret Miles, already at work. This committee, which meets in private and heard Mr Charles Curran, director general of the BBC, at its session this week, intends to tackle the broad kind of question that the Annan Committee might have done. It will consider the relaxing of the monopolies of the BBC and the ITA, for example, and will also compare British television with services abroad.

The 76 Group, founded several years ago by discontented television professionals within the BBC and ITA, is about to announce the formation of its own independent inquiry into the future structure of British television. The group, now led by Mr Philip Whitehead, MP, and including Mr Stuart Hood and Mrs Doreen Stephens, formerly of the BBC, was instrumental in leading to the establishment of the Annan Committee.

The Action Society Trust will also wade into the subject and, convinced (as is the 76 Group and many critics), that the TAC's report was inadequate, may concentrate on the new technical developments in communication that Britain should now begin to consider. Yet another inquiry is just being completed by the General Synod of the Church of England. Its emphasis has been on possible changes in religious broadcasting.

Perhaps a more critical question than whether there will be an inquiry or not is how seriously Sir John Eden takes the TAC's report. He has visited the United States recently and should be aware of the contrast between the cable television there and the vagueness about it in the United Kingdom.

Roskill Disinterred

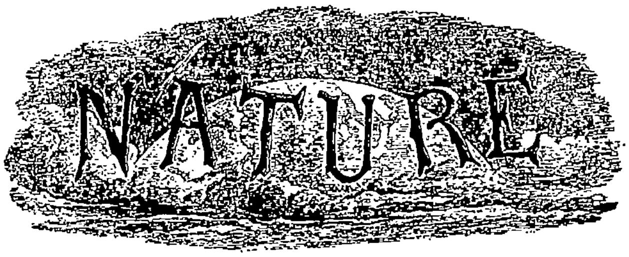
THE British Government appears to be having second thoughts about the decision, itself much delayed, to build a third international airport for London in the Thames estuary, on Maplin Sands. In response to protests from the Opposition and many of its own supporters in the House of Commons that the airport is a potential environmental nuisance, and unnecessary as well, the government has decided that the bill authorizing developments at Foulness should be sent to a Select Committee of the House of Commons—a procedure that will allow reasoned objections to be made by outside interests but which is almost certain to delay a final decision until much later in the year. In the circumstances, it is no surprise that local authorities such as the Liverpool City Council are asking that consideration should be given to the development of an existing provincial airport instead of the development proposed in the Thames estuary, and no doubt this would be a convenient way of shedding some of the burden on local rates. It is more surprising that Mr Anthony Crosland, the Opposition's spokesman on environmental matters, should have lent his support to a reconsideration of the Foulness decision, for it was his sleight of hand which originally diverted the government and the British Airports Authority from swallowing the recommendation of the Roskill commission that the third airport should be built at Stansted.

The decision about the third airport is not merely a parochial matter but a teasing issue in environmental management. There are two questions to be decided—when will a third airport be needed and where should it be put? The Roskill commission estimated, in 1971, that existing airports around London would be saturated by 1981 and that, by 1983, the cost of diverting aircraft from crowded airports would exceed the financial benefits to be gained by delaying a decision on a third airport. Its own preference was for a third airport to be in service by 1980, if only because of the danger that traffic might grow more quickly than had been forecast. In the event, however, the past two years have not been quite as bullish as originally foreseen. In the circumstances, there is at least good reason why the House of Commons should now take another look at the growth of traffic into the London area, and it is just conceivable that a decision could fairly be postponed until 1974, at least if those who live near the existing airports are prepared to tolerate for another year the nuisance to which they are already subjected.

The location of the new airport is a more contentious issue. Few would deny that Foulness is the best of all the sites in the neighbourhood of London considered by the Roskill commission. It would be a nuisance to fewer people than any other new airport in the metropolitan area. Moreover, its cost is only marginally and even problematically greater than that of an inland site, while there are obvious possibilities of grafting on to an airport in the Thames estuary industrial and commercial facilities which would be thoroughly unwelcome elsewhere. So much seems clearly to be recognized by the local authorities directly concerned, who appear to welcome the prospect of a development at Foulness. But there are, of course, some important disadvantages of the site. Several miles of mud flats will be replaced by artificial reclamation. Some but not all of those who live nearby will be afflicted with uncovenanted nuisance and there is even a possibility that the development of a major airport in south-east Essex will permanently change the character of what has previously been in part a rural area. On balance, however, if the need for air transport and the prospect of continued growth are acknowledged, it seems inevitable that the development at Foulness should go ahead—and luckily, the sense of injustice from which local inhabitants may suffer should at least be made less acute by the Conservative government's more liberal legislation on compensation for those adversely affected by public works. In this sense, the issue boils down to a simple conflict between the needs of the community as a whole and the interests, legitimate though they may be, of those who live nearby and who happen not to want an airport there. The House of Commons will do its reputation further damage if it fails to inform the coming argument about a third London airport with this simple and familiar principle.

But is there any chance that the need for a third London airport could be made as if by magic to go away? The Roskill commission was prevented by its terms of reference from considering more radical alternatives to the development of a third airport—Shannon in the Republic of Ireland or one of the possible sites in France might, for example, be as suitable as international feeder terminals as Liverpool. It is entirely conceivable that such terminals would be a more efficient means of helping people to embark on international journeys, especially if steps were also taken to rationalize the timetables of the international airlines, which at present compete for peak hour traffic and in the process exaggerate the problems of existing airports at these same times. The trouble is that any such solution to the problem of how to carry passengers to destinations in the United Kingdom would require not merely a reorganization of the relationships between governments and the commercial airlines but the development of inter-city air traffic within Britain on a scale not yet foreseen. Whether the environmental nuisance would thereby be reduced is anybody's guess, but the outlook is not cheerful. And certainly there is no prospect that these complicated matters could be tackled in time to meet the demand for air travel in the early 1980s.

100 Years Ago



Inherited Instinct

THE following letter seems to me so valuable, and the accuracy of the statements vouched for by so high an authority, that I have obtained permission from Dr. Huggins to send it for publication. No one who has attended to animals either in a state of nature or domestication will doubt that many special fears, tastes, &c., which must have been acquired at a remote period, are now strictly inherited. In the following case we see a specialised feeling of antipathy transmitted through three generations of dogs, as well as to some collateral members of the same family, and which must have been acquired within a very recent period. Unfortunately it is not known how the feeling first arose in the grandfather of Dr. Huggins's dog. We may suspect that it was due to some ill-treatment; but it may have originated without any assignable cause, as with certain animals in the Zoological Gardens, which, as I am assured by Mr. Bartlett, have taken a strong hatred to him and others without any provocation. As far as it can be ascertained, the great-grandfather of Dr. Huggins's dog did not evince the feeling of antipathy, described in the following letter.

CHARLES DARWIN

"I wish to communicate to you a curious case of an inherited mental peculiarity. I possess an English mastiff, by name Kepler, a son of the celebrated Turk out of Venus. I brought the dog, when six weeks old, from the stable in which he was born. The first time I took him out he started back in alarm at the first butcher's shop he had ever seen. I soon found he had a violent antipathy to butchers and butchers' shops. When six months old, a servant took him with her on an errand. At a short distance before coming to the house, she had to pass a butcher's shop; the dog threw himself down (being led with a string), and neither coaxing nor threats would make him pass the shop. The dog was too heavy to be carried; and as a crowd collected, the servant had to return with the dog more than a mile, and then go without him. This occurred about two years ago. The antipathy still continues, but the dog will pass nearer to a shop than he formerly would. About two months ago, in a little book on dogs published by Dean, I discovered that the same strange antipathy is shown by the father, Turk. I then wrote to Mr. Nichols, the former owner of Turk, to ask him for any information he might have on the point. He replied—'I can say that the same antipathy exists in King, the sire of Turk, in Turk, in Punch (son of Turk, out of Meg) and in Paris (son of Turk, out of Juno). Paris has the greatest antipathy, as he would hardly go into a street where a butcher's shop is, and would run away after passing it.

WILLIAM HUGGINS

From Nature, 7, 281, *February* 13, 1873.

OLD WORLD

Euratom Reprieved at Dawn

At a fourteen-hour meeting that ended at 6 o'clock on Tuesday morning the nine science ministers of the European community finally agreed a four-year programme for Euratom.

The three-part agreement, which will cost a total of 160 million units of account (about £66 million), puts an end to the five years of uncertainty about Euratom's future.

The compromise agreement will save the jobs of 1,650 of the staff of the four joint research laboratories at Ispra in Italy, Karlsruhe in West Germany, Geel in Belgium and Petten in Holland, the last of which was under threat of closure.

The four-year formula provides that 140 million units of account will be spent on a common programme of advanced technology projects ranging from environmental work to applied data processing and reactor safety.

Although this programme is common, not all nations will participate in all parts of the project. Work on the Petten high flux reactor will be shared between Holland, Belgium and West Germany only, France will not be involved in work on the control of fissile materials and Italy will not contribute to research on plutonium at Karlsruhe. Otherwise the programmes in this part of the package are common. In all 1,440 staff will be employed on the first part of the settlement.

The second part of the package has an agreed budget of 20 million units of account and will provide work for a further 209 staff, but the precise research to be undertaken has not yet been agreed. About a dozen projects have been put forward by the commission under this heading, and the nine nations have to agree by May which of these they will support. Ispra's work on the use of hydrogen to generate energy is one of these optional projects.

The third part of the package is labelled "indirect action programmes" and deals with contributions that Euratom will make to various national research projects in the enlarged community. These also will be decided by the end of April and a number of Euratom staff will be seconded to national laboratories, a move that will help reduce redundancies.

The second part of the formula will be reviewed annually and the first part after two years, thus providing at least a measure of security for the 1,948 staff of Euratom, many of whom were threatening to stage a "work-in" on the lines of the Upper Clyde Shipbuilders unions if agreement on a realistic programme was not reached.

As it is, 98 of Euratom's scientists and administrative staff will be made redundant. Forty-eight of these will go because the programme has been cut from the five-year agreement that the commission wanted instituted; the remainder will make way for staff from Britain, Ireland and Denmark who only became part of Euratom in January.

The final programme is evidently something of a compromise between the commission's plans—which would have produced a budget of 185 million units of account—and the views of Britain, Holland and France who were eager that Euratom should be pruned down.

Reactions from the ministers concerned were those of relief as they ended their lengthy meeting. The Belgian science minister, Mr Charles Hanin, said, "it has been a good night and we are at last emerging from a situation which has lasted many years". Mr Ralf Dahrendorf, the commission member who now has the unenviable task of actually putting the agreement into effect, was slightly more cautious. "This is a sort of turning point", he said.

NUCLEAR POWER

Vinter Report: Select Committee Acts

The Select Committee on Science and Technology is to invite Mr Tom Boardman, Minister for Industry, to appear before it with a copy of the Vinter report to explain why the report cannot be published.

Officially known as the thermal reactor review and compiled under the chairmanship of Mr Peter Vinter, deputy secretary at the Department of Trade and Industry, the report is intended to help ministers decide which type of reactor should be built next.

The Select Committee, which has been examining the nuclear power industry for some months, has repeatedly asked that the report be published. Now it has attempted to use its right to send for "persons, papers and records", as the government has refused to part with a copy.

The committee—which last year published the Docksey report which the government had refused to make public—believes that there is an important principle at stake. It is quite willing to respect the commercial secrets in the Vinter report that the government has repeatedly cited as its reason for not publishing, but it feels that the government's refusal to divulge the thinking that lies behind the report is obstructing the committee in its work.

Mr Arthur Palmer, chairman of the subcommittee that is examining the nuclear power industry, made the point forcefully when the committee was taking evidence from the United Kingdom Atomic Energy Authority last week. On hearing from Mr F. J. Doggett, deputy chairman of the authority, that the authority knew of the Vinter report's contents, he rejoined that he hoped people would note that a public corporation has information that has not yet been made available to Parliament.

Mr Doggett, questioned on the reorganization of the nuclear industry that the government has promised, said that one of the first tasks of the new company will be to establish links with a European company. The new company, he said, "should be left free to choose the best common partnership".

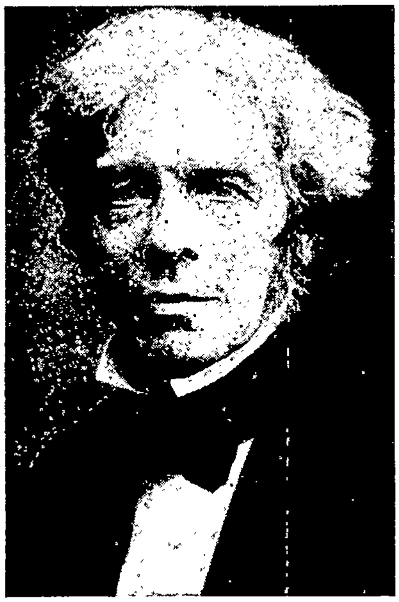
Mr Doggett's emphasis on European links reflected the views of Sir Edwin MacAlpine, chairman of the Nuclear Power Group, when he gave evidence to the select committee recently. Sir Edwin was also at pains to urge that the new company "should be free from any influence of manufacturers"—a remark that was taken to be a thinly-veiled reference to the government's apparent intention to install Sir Arnold Weinstock, managing director of GEC, at the helm of the new company. GEC supplies turbogenerators and other equipment for some nuclear contracts. Sir Edwin made it clear that he favoured a new company made up of three parts—his consortium, the Atomic Energy Authority, and the other consortium, British Nuclear Design and Construction, of which GEC is a part. The government, however, is believed to favour a company with strong central management rather than a merging of the consortia on the lines proposed by Sir Edwin. Sir Edwin, however, told the committee that as far as hopes for a European company go, it "would be a terrible disaster if any one company were seen to be in control".

HISTORY OF SCIENCE

Faradaylia

MORE than 105 years after his death, the Royal Institution has finally paid tribute to Michael Faraday. Earlier this week the Queen, the Royal Institution's patron, opened a museum, an archive room and a refurbished laboratory, all bearing Faraday's name.

Professor Sir George Porter, the institution's director, repeated Faradays' chief experiments on electricity—including, with commendable energy, a hand-driven demonstration of electromagnetic induction with a light bulb, a coil and an iron bar—and the Queen unveiled a plaque on the floor below, initiating the curtain motor by an impulse from the original iron ring used by Faraday when he discovered electromagnetic induction. The ring worked, the curtain drew back and everyone applauded.



Michael Faraday

The Royal Institution has presented its treasures well. Probably the most complete collection of the work of one scientist, the Faraday museum contains models of the first electric motor, examples of early generators of Faraday's time, apparatus made by Newton for Faraday and such items as his "electric egg" used for the study of discharge in gases at different pressures. The archives room contains Faraday's diaries, all 16,000 entries, each one of which added something to scientific knowledge, and a copy of the probate of his will in which he wrote of his manscripts " . . . these I offer for the library of the Royal Institution, if my managers should think them worth a place; if not they remain at the disposal of my executors".

The archives also contain manuscripts of Davy, Tyndall, the Braggs, T. H. Huxley and Spottiswoode to name but a few. But the highlight of the displays is a reconstruction of the small laboratory in which Faraday made most of his discoveries. The room has been returned as far as possible to its nineteenth century appearance, with pieces of Faraday's apparatus dotted about the place, including the great horseshoe electromagnet he built. It is cleverly done, carefully lit, and looks as though Faraday has just left the room for a moment.

The Royal Institution may have been a long time making its Faraday collection available to the public, and it may be all of five years since the Faraday Centenary Appeal raised the money to carry out the transformation of the laboratory (in the form of a gift from the Camille and Henry Dreyfus Foundation), but it has been worth the wait.

HORTICULTURE

Mercury Substitute

A DEVELOPMENT which obviates the need to use compounds of mercury to dress seeds has been turned to commercial use by scientists at Rothwell Plant Health in Lincolnshire.

Traditionally, seeds have been dressed with mercury compounds before planting to avoid diseased crops. But even though the amounts of mercury compounds used worldwide for agricultural purposes are small—in 1968 slightly more than 2,140 tonnes were used, 1,600 tonnes in Japan, 400 tonnes in the United States and only 20 tonnes in Britain—there has been concern about the health of the people who carry out the dressing process.

During recent years there have been several attempts to develop a seed dressing as effective as mercury which is not toxic, and the dressings which have been developed were found to be effective for a particular variety of seed, but, generally speaking, no universal substitute for mercury has been marketed until recently.

In 1972, Rothwell Plant Health Limited of Lincoln marketed a dressing composed of a mixture of carboxin and thiram which, it is claimed, is as effective as mercury in preventing disease in cereal crops. But to buy a ton of seed dressed with the non-mercurial dressing costs £4 more than the mercury dressed seed. At present a farmer who wishes to buy a ton of wheat seed will probably pay about £60 or £64, depending on the dressing used.

Rothwell is also developing a hybrid wheat variety. Mr Giles Dixon, director of scientific development at Rothwell Plant Breeders, said recently that the aim is to produce an F_1 hybrid with a yield 25 per cent greater than non-hybrid varieties at the time that the hybrid would be sold commercially. Mr Dixon also said that it would probably be five years before it was known whether the hybrid variety would be commercially viable.

SCIENCE MUSEUM

Props for the Provinces

A FUND of £150,000 has been set up by the government to help needy provincial museums to purchase and install scientific and technological material.

The fund is to be administered by the Science Museum and becomes available on April 2 this year. Its aim is to establish gradually a national pattern of acquisitions, avoiding unnecessary duplication and encouraging regional museums to build up specializations in subjects related to the particular industries and interests of their areas.

The terms of reference of the fund are broad. Any object of scientific or technological interest is covered—including those relating to the biological and geological sciences—and transport, restoration and installation all qualify for financial support.

Miss Margaret Weston, the Science Museum's new and young director, said this week that the fund, which is designed to avoid the loss of technological and scientific material that has taken place in recent years, "will help a lot", and she is looking forward to seeing what kind of material the provincial museums wish to save.

The fund is the result of a report presented nearly two years ago by the Standing Commission on Museums and Galleries which recommended that £200,000 a year should be made available to help the provincial museums. Although the Paymaster-General has only approved £150,000 for the first year, Miss Weston points out that the grant is renewable each year and may well be increased.

The granting of money to provincial museums is a matter in which science has lagged behind the arts. The Victoria and Albert Museum has had a similar scheme running for several years, and although it was quite willing to consider scientific and related objects, this is the first time a strictly scientific fund has become available.

When considering applications, Miss Weston said this week, the Science Museum will consult with the Geological Museum and the National Maritime Museum where necessary. Initial reaction among provincial museums is enthusiastic.

A hidden bonus for the Science Museum is that the new fund throws into greater relief the Science Museum's current acquisitions grant, which is a paltry £8,000 a year. "That," says Miss Weston, "will have to go up." But not yet. The museum's budget is run on a quinquennial basis and there are still eighteen months to go before the new settlement is due.

UNIVERSITY RESEARCH

Physical Sciences Cut

THE growth of postgraduate numbers in the physical sciences is to be heavily restricted following the government's white paper on education published last November.

Now that the University Grants Committee has apportioned the £1,392 million (1972 prices) of recurrent grant that makes up the 1972–77 quinquennial settlement, certain of the white paper's provisions have become clearer, in particular the stipulation that the numbers of postgraduate students are to be cut from the current 19 per cent of full-time students to 17 per cent. This amounts to a 60 per cent reduction on the extra numbers of postgraduates requested by the vice-chancellors in their submissions to government.

Vice-chancellors are seriously concerned at this cut in the growth rate which will increase Britain's postgraduate numbers by only 7,000 to 52,000 by 1976–77, and they are also critical of the way post-experience courses, taught postgraduate courses and research degrees have all been lumped together in the calculations.

Guidance as to the numbers of postgraduates in each subject area that individual universities should aim at has been given to the universities by the UGC, and from these figures it is apparent that science and technology have suffered badly from the reduction in growth, physics and chemistry taking the largest cuts, with medicine, social sciences and business studies receiving the largest increases in postgraduate numbers.

A number of vice-chancellors are also seriously worried by government advice, issued through the UGC, that growth in the numbers of overseas postgraduate students taken by British universities should also be cut. Many of these come from the third world and it is felt that training overseas postgraduates in skills that can be used in their own countries is one of Britain's most helpful contributions to the developing nations.

The vice-chancellors also maintain that the universities must be given full compensation against inflation during the quinquennium. The settlement is a particularly tight one with the universities being asked to take more students at lower unit costs, and the vice-chancellors feel that this can only be done if inflation is not allowed to further cut the actual monies available.

SPACE

ELDO Lingers On

THE European Launcher Development Organization won a two-month reprieve at a council meeting in Paris last week. The council decided to keep the Europa II programme running until April 1 after France and Germany had again failed to agree over the long-term continuation of the programme.

Europa II is all that is left of the ELDO programme after the decision of the European Space Conference in December last year (see *Nature*, **240**, 516 ; 1972) to scrap Europa III in favour of a new French launcher proposal, L3S, which the French claim will be considerably cheaper than Europa III would have been.

The Europa II programme consists of two test firings during this summer and autumn, the second of which will carry a dummy load to represent the communications satellite Symphonie I.

Two firings of Symphonie are then planned, followed by a launch of an ESRO satellite to complete the Europa II programme. The French are eager to see the programme through, but the Germans are believed to favour scrapping the launcher, which has proved a costly failure so far, preferring instead to send Symphonie up on an American Thor Delta launcher.

Last Friday's meeting did little to produce any solution to the disagreement, but the council did agree that the Europa II programme is to continue as planned until April 1. A final decision on the future of the programme, and therefore of ELDO, will be reached "in good time" before then.

ELDO's future as a separate organization is in any case limited. The European Space Conference held last December agreed to a British proposal that a European Space Agency be formed by 1974. Under this proposal ELDO is to be merged with ESRO under the control of the agency which will also oversee individual space programmes of the member countries. It is expected that this new agency will also be responsible for developing the L3S, a three-stage launcher which the French claim will have the same performance as Europa III but at a cost of Fr 2,200 million (about £180 million) compared with the estimated Fr 3,000 million that Europa III would have cost (see *Nature*, **240**, 434; 1972).

HOVERTRAINS

New Linear Motor

IT is now feasible both to levitate and to propel a hovertrain using only a linear induction motor. This was the crux of the Friday evening discourse delivered last week at the Royal Institution by Professor Eric Laithwaite, of Imperial College, London, one of the founding fathers of the linear motor.

Professor Laithwaite backed up his assertion by demonstrating the latest version of the transverse flux motor. This kind of motor, in which the flux is perpendicular to the direction of motion rather than along it, was evolved by Professor Laithwaite, Dr J. F. Eastham and the Imperial College group in 1968 and developed since then.

Although the new motor was first exhibited at a high speed transportation exhibition in the United States last year, the details were revealed for the first time last Friday. The unveiling is particularly timely because of the extreme uncertainty at present about the future of Tracked Hovercraft Limited, the wholly owned subsidiary of the National Research Development Corporation, which has now developed a hovertrain weighing ten tons, supported on an air cushion and propelled by a linear motor. This vehicle recently achieved a speed of 107 miles an hour on the company's 1-mile test track in Cambridgeshire ; the average acceleration on this occasion was ⅓ g.

The government has not yet decided whether or not to inject another £4 million into the hovertrain project, but Professor Laithwaite said this week that for this amount of money it would be quite possible, using the new motor, to build a 30-ton vehicle capable of carrying passengers and travelling at 250 miles an hour within three years. This would involve lengthening the test track to 3 miles. Professor Laithwaite also says that such a vehicle could hover at a height of 6 inches above its track. The present British hovertrain, the RTV 31, travels along with a clearance of only an inch or two.

Research on high speed transport of this kind is being actively pursued in several other countries, the United States, France, Germany and Japan for example. But whereas most people seem to be agreed that the linear motor, in some form, is an essential ingredient of any arrangement, there are differences of opinion about how vehicles should be made to hover. Germany favours a suspension system involving a feedback loop to maintain stability, whereas the United States, France and Japan are putting their money behind levitation based on superconducting magnets. Both these systems suffer from the disadvantage that they will probably prove much more expensive (in liquid helium for example) than a system that makes use of a transverse flux linear motor and thus requires no separate means of levitation or suspension.

CREATIONISM

Backing the Bible

One group in Britain that has been watching the activities of the California and Michigan State Education Boards' activities with more than average interest recently is the Evolution Protest Movement. The move by the two education boards to include the religious theory of creation (albeit in a very cursory form) in school textbooks has met with the cautious approval of the movement, which, since 1932, has been dedicated to the thankless task of getting British scientists and laymen to listen to its views.

The movement, which has 800 subscribing members, has three chief aims —to demonstrate that the theory of organic evolution is not in accordance with scientific fact, to show that evolutionary teaching causes a decline in true Christianity and to supply information supporting the Bible statements on creation as opposed to the widely accepted views of evolution. Their chief weapons are the book and the pamphlet, although members of the movement are always willing to lecture and debate anywhere.

Since 1932, when the movement was founded by Captain Ackworth, RN, a submarine commander who is reputed to have won a libel action against Churchill, more than 200 pamphlets and several books have been published by the movement, the lodestar of their work being Professor W. R. Thompson's introduction to the 1956 Everyman edition of *The Origin of the Species.* Certainly better argued and less discursive than most of the movement's work, Thompson's critique forms part of the scientific backbone of what is essentially a lay organization. Past presidents include Douglas Dewar, a one time auditor general of India, Sir Ambrose Fleming, the British physicist who first devised the electron tube, and Captain Ackworth, although the current president, Sir Cecil Wakeley, past president of the Royal College of Surgeons, is a man highly distinguished in a biological field.

Dr C. E. A. Turner, the movement's chairman, a retired chemistry schoolmaster with an interest in biochemistry and a doctorate in the history of scientific education, says that the movement's chief concern is to see "the other side" of the Darwinian coin put across. The movement imposes no set beliefs on its members, simply a generalized opposition to Darwinism, and Dr Turner is at pains to point out that he does not want to see the creationist theory imposed on schoolchildren. "We want to see that people are aware of the alternatives; the problem at present is that one side is pushed to the exclusion of the other." Dr Turner also complains that "it is very hard to get anything into the press. If you write as a member of the movement people think you are cranky—classed with the flat-earthers or something—and as there are a number of competent scientists in the movement this is not fair".

EPM has links with the Creation Research Society in the United States, a body of research scientists in a number of disciplines who attack Darwinism on more strictly scientific grounds, although they are "committed to a full belief in the Biblical record of creation and early history".

EPM is a much more modest organization, producing its half yearly journal with pamphlet supplements, and holding its annual meeting each September. But membership has gradually increased and the present wave of controversy in California and Michigan, not to mention the correspondence columns of *Nature,* could give it the chance to make its views better known, although it has at present no plans to seize the day.

SOVIET SCIENCE

Luna-21 Lands

from our Soviet Correspondent

The landing of Luna-21 and roll-out of Lunokhod-2 into the Mare Serenitatis area, at a site some 180 km almost due north of the Apollo-17 site, is already being hailed by the Soviet press as a precursor of cooperation in space between the United States and the USSR.

This international theme of Lunokhod-2 is also stressed by the presence of a directional laser reflector supplied by France which extends the joint Franco-Soviet research on measuring accurately the distance from Earth to Moon begun by Lunokhod-1 (*Nature,* **228**, 795; 1970).

Although a full list of experiments has not been announced, the programme of Lunokhod-2 seems a repetition of that of its predecessor, including a spectrometer to determine the chemical composition of the surface of the Moon, a twin-channel directional photometer to analyse radiation from stars in the visible and near ultraviolet region (similar to those carried by Kosmos 51 and 213), a magnetometer experiment, instruments to test the mechanical properties of the surface of the Moon including a conical rotary penetrometer with cruciform blades and sensors attached to the chassis of the vehicle to measure the angle of inclination.

There are also panoramic television cameras with angles of vision 180×30° in the lateral and 360×30° in the vertical direction. The fact that Lunokhod-2 on its roving mission has covered more than 1,100 m in the first 4 days, compared to Lunokhod-1 which moved a mere 125 m in the same time, indicates the emphasis placed on gathering as many photographs as possible from this transitional sea-to-highland area. And, once again, as in Lunokhod-1, the ambient conditions of the instrument chamber (temperature 20° C, pressure 80 cm Hg) suggesting a life support system, may be some indication that the instruments on board have been designed for use in manned missions.

IMPERIAL COLLEGE

Unemployed Scientists

Imperial College still retains its attraction for undergraduates in the sciences and engineering. In the college's annual report published recently, it is reported that 4,994 students applied for a total of 952 places at the college for the academic year 1971–72. But this figure is 12.1 per cent fewer than applied the previous year.

True to tradition, Imperial College still boasts one of the largest postgraduate bodies in Britain with 37 per cent of the students during 1971–72 involved in either research or doing advanced courses.

But in spite of the reputation of the college its graduates still found difficulty finding jobs. A survey shows that in December 1971, 5 per cent of that year's Imperial College graduates were unemployed and that the whereabouts of 7.3 per cent were unknown. In September 1972 the University Grants Committee published equivalent figures for the country as a whole (*Nature,* **240**, 175) and it reported that 7.9 per cent of all 1971 graduates were unemployed in December 1971—with 6.7 per cent of applied science graduates still without a job.

In common with science graduates of other colleges and universities, Imperial College students had to diversify to find employment. The report says that some scientists and engineers now find employment in accountancy, banking, the actuarial profession and the Stock Exchange and that in 1971 13.1 per cent of the college's first degree students took up employment in legal, commercial and related areas compared with 3.1 per cent in 1965. Even 10.9 per cent of the college's higher degree graduates now find their way into these fields compared with 0.8 per cent in 1965.

But Imperial College has made efforts to improve the situation and during the past year the college's appointments board has set up contacts with companies in Europe and has increased contact with British companies by the simple expedient of arranging for members of the academic staff to hold consultancies in industry.

NEW WORLD

New Hope of Comprehensive Test Ban?

by our Washington Correspondent

THIS year marks the tenth anniversary of the signing of the treaty banning the testing of nuclear weapons in the atmosphere. It also marks the end of a decade of intensive underground testing and a decade of discussions and research concerned with extending the partial test ban to include all methods of testing nuclear weapons. But, while the governments of the United States and the Soviet Union have repeatedly reaffirmed their commitment to "seek to achieve the discontinuance of all test explosions of nuclear weapons for all time", a commitment enshrined in the preamble to the partial test ban treaty, they have not even come close to agreeing on a formula for implementing such a comprehensive agreement.

Early next week, however, a group of some two dozen senators, led by Kennedy, Mathias, Hart, Humphrey, Muskie and Case, will introduce a resolution into the Senate calling on President Nixon to set forth a new proposal for a permanent comprehensive test ban treaty. And, in the meantime, the resolution urges the President to propose a moratorium on weapons testing, to remain in effect as long as the Soviet Union also abstains from underground testing. The resolution calls for such steps because "early achievement of total nuclear test cessation would have many beneficial consequences; creating a more favourable international arms control climate; releasing resources for domestic needs . . . and complementing the ongoing strategic arms limitation talks".

Few would disagree with those sentiments, but the critical question is no longer whether or not a comprehensive test ban is desirable but whether it can be monitored and enforced with maximum assurance that it is not being breached, and without generating false alarms. That has always been the stumbling block in the path of negotiations towards such a treaty, and it will certainly become the central point in discussions on the Senate resolution.

The Administration is, however, now undertaking a fresh and important initiative to extend the theoretical basis for ensuring that a comprehensive test ban could be adequately monitored. The initiative involves improving the capabilities of some 20 seismic recording stations in the World Wide Standard Seismographic Network (WWSSN) —a network of seismographs around the world managed at present by the National Oceanic and Atmospheric Administration—and the installation of up to three long-period seismic arrays in locations which have yet to be firmly decided. Such an upgrading of seismic recording capabilities was in fact proposed by the United States delegation to the Committee on Disarmament in Geneva last year, and planning is proceeding along the lines set out in the US working paper presented to the committee.

Upgrading of the WWSSN stations, which will be financed by the Defense Department's Advanced Research Projects Agency (ARPA), will consist of equipping the stations with digital recording facilities, moving some to sites where they are less affected by background "noise" signals from the weather, traffic and other factors and in some cases by installing improved instrumentation. Another development will be more efficient transfer of data from the seismic stations to a storage and analysis centre in Virginia; data from some stations will be relayed by satellite to the United States. Planning is now in the final stages and the upgradings are expected to be carried out within the next few months.

The immediate objective is to pro-

MILITARY FITNESS

Sickle Cell Screening

by our Washington Correspondent

A COMMITTEE working under the auspices of the National Academy of Sciences has recommended that all potential recruits for the military services should be screened for sickle cell anaemia. Those who are found to have the disease should be excluded from service, but those who are found to carry only the sickle cell trait—the recessive gene mutation which generally poses little or no hazard to the carrier—should not be excluded. The committee's report, although it applies specifically to military policy, is an important statement in the growing controversy which surrounds screening policies for sickle cell anaemia.

The National Academy of Sciences was asked to draw up recommendations for the Department of Defense last year, and the chief conclusions to emerge from the resulting study are, first, that screening for sickle cell disease and for the trait should be carried out on every recruit, regardless of race; second, that it should be one part of a battery of tests for other genetic disorders; and, third, that potential risks associated with the trait are so small that there is no need to exclude carriers from any military duty except for piloting aircraft.

Federal, state and local genetic screening programmes designed to identify those who have sickle cell disease and those who carry the sickle cell trait have generated considerable controversy for several reasons. One complaint is that, since the disease is largely found among the black population, many screening programmes require the compulsory testing of blacks but not of whites. The disease and the trait can, however, show up among whites—particularly those of Mediterranean origin—and such screening programmes have been criticized on racialist grounds. Another common complaint is that, although possession of the trait involves little or no hazard to the carrier, those who show up positive in the tests are being discriminated against, for example, in paying higher insurance premiums. Finally, it is often argued that, since the chief reason for screening for the sickle cell trait is to advise couples on the risks associated with having children, it serves little purpose to tell a child that he or she carries the trait.

Many of these considerations have been brought sharply into focus by a recent report on four military recruits who died during training at high altitudes for no apparent reason. Each was, however, subsequently found to be a carrier, and possession of the sickle cell trait has thus been implicated in their deaths. But the NAS committee found that the evidence to link possession of sickle cell trait with sudden death is entirely circumstantial. According to Dr Robert F. Murray, chairman of the committee, "it is guilt by association", and the report suggests that "there must be other, yet unknown contributory factors, not necessarily related to the sickle cell trait, that make some persons susceptible to collapse and/or sudden death". For this reason, the committee recommends that sickle cell trait carriers should be excluded only from serving as pilots, where they may be subjected to low pressure or other unusual conditions. But the committee also acknowledges that this recommendation is conservative.

vide a better data base from which to assess the potential capabilities of a network of seismometers around the world for policing a test ban, and in particular to try to ascertain how great the problem of false alarms—shallow focus earthquakes whose seismic characteristics look like explosions—will be. But the upgrading will also provide a welcome benefit for geophysical research, for the data from the upgraded stations will be available to the seismological community in digitized form so that they can be handled immediately by computers. At present, much time is taken up in transcribing film records from WWSSN stations into digital form. The higher quality data which are likely to come from the quieter sites and improved instrumentation will also be greeted with enthusiasm.

But will upgrading the WWSSN stations bring a comprehensive test ban treaty any closer? First, it is important to realize that the upgraded system is intended to be a research system, and not a surveillance system to police a test ban. Nevertheless, it could provide an important mass of data to help iron out some of the seismological problems that still remain in discriminating between small earthquakes and low yield explosions.

Briefly, both earthquakes and explosions produce a variety of seismic waves which travel through the body of the Earth (body waves) and along its surface (surface waves). Research aimed at discriminating between earthquakes and explosions has concentrated on measuring the proportion of energy from an event generated in the form of long period surface waves (M_s) and short period body waves (m_b). It turns out that, in general, earthquakes are more efficient generators of surface waves than are explosions, and the so-called $M_s:m_b$ discriminant is usually sufficient to tell them apart. The focal depth of the event is also a powerful discriminating factor, for those which take place deeper than a few kilometres can automatically be classed as earthquakes.

But there are a few earthquakes each year which for some reason do not generate the predicted proportion of surface waves, and they are liable to be incorrectly classified as explosions. The reasons for such anomalous earthquakes are not well understood, nor is it possible to predict with certainty where such events may occur. More light may be shed on this problem by upgrading the WWSSN stations.

Correction

In the note "Belt Tightening in Store for US Science" (*Nature*, **241**, 303 ; 1973), the figure of $87 million in the last paragraph of column 1 on page 304 should have read $87,000 million.

There is also the problem of the ever present background noise which limits the ability of seismometers to pick up signals from very small earthquakes or explosions. Seismometers installed at any site will record ground slippage and earth movements resulting from atmospheric conditions, traffic and other factors, and such interference can never be eliminated entirely. This has two important consequences. The first is that seismic signals from a very small explosion would be lost in the background noise, and a test ban treaty would have to be negotiated with this in mind, and the second is that it may be possible for a determined violator of such a treaty to use a variety of means for depressing the signals from larger explosions so that they too would be masked by the background noise, or hidden in the signals of large earthquakes.

All these considerations were brought out during hearings held in November 1971 by the Joint Committee on Atomic Energy (see *Nature*, **234**, 6 ; 1971). And at that time there was considerable discussion of the ultimate capability of a seismic network for detecting and discriminating between explosions and earthquakes. The estimates ranged between a detection threshold of about $m_b=4.0$ (equivalent to an explosion of one or two kilotons fired in solid rock) to about $m_b=4.75$. It was also made clear during the hearings that the problem of anomalous events increases markedly the smaller the event.

The joint committee itself, whose support will be a key factor in determining whether there will be negotiations for a test ban, was also concerned about the ways in which a determined violator could escape detection under a test ban. But at least one key member of the committee has become convinced that a test ban should now be negotiated, for Senator John Pastore, who was chairman of the joint committee in the 92nd Congress, is a co-sponsor of the resolution to be introduced into the Senate next week.

The chief stumbling block in negotiations for a comprehensive test ban has always been the insistence by the US government that seismic means alone are not sufficient to police such a treaty, and that on-site inspection is required as an ultimate assurance against violation, and the insistence by the Soviet government that on-site inspection is not needed. The official US position is unlikely to change until the Department of Defense is reasonably satisfied that a test ban could be adequately policed by seismometers, without a great false alarm problem, and without too great a risk of evasion. Upgrading the WWSSN stations and deployment of new long period arrays could be a step towards that goal.

NOAA

False Promises

by our Washington Correspondent

Although the scientific community is by now attuned to the fact that political rhetoric is infrequently followed by hard cash, officials in the National Oceanic and Atmospheric Administration's earthquake and hurricane modification programmes are understandably feeling hard done by. Earthquake research and hurricane control, it should be remembered, are part of the Administration's much publicized drive to bring the forces of science and technology to bear on problems affecting society ; and the 1973 budget, sent to Congress a year ago, promised large increases in funding for NOAA's work in these fields. Instead of largesse, however, many of the programmes have been given the axe.

In short, NOAA has been forced by financial stringencies to get out of the business of earthquake prediction, earthquake hazards assessment and earthquake engineering, give up its management of the National Earthquake Information Center and the Worldwide Standard Seismographic Network (WWSSN) and suspend the chief hurricane modification programme, Project Stormfury. Many of the earthquake programmes will be transferred from NOAA to the US Geological Survey in the Department of the Interior, but at the beginning of this week a plan for the transfer was awaiting approval by the Office of Management and Budget. The idea is to save money by consolidating NOAA's geophysics and geomagnetism operations with those of the USGS.

The plan for saving most of NOAA's seismology and geomagnetism facilities has been agreed to by officials of the National Science Foundation, the US Geological Survey and NOAA, but approval by the Office of Management and Budget is needed before it can be put into effect. In any case the transfer will probably not take place until the end of June. Essentially, the plan would leave NOAA with responsibility for only three seismic observatories needed for the tsunami warning system. Nearly all the rest of its seismology and geomagnetism operations would be transferred to the USGS and the National Science Foundation would provide some of the money for operating them. Since the Geological Survey also runs a large earthquake research programme, the idea would be to consolidate facilities, and thus to save money.

Seismologists in universities will be anxious to see that data from seismological observatories will still be readily available under any new arrangements. This is what has tentatively been decided: the National Earthquake Information Center, which issues data on the preliminary location of epicentres of seismic events around the world, will be transferred to USGS, but more complete data will continue to be available from NOAA's Environmental Data Service. In other words, seismology data will be available from the same sources, but half will be managed by USGS and the rest by NOAA. Small wonder that one NOAA official described the whole situation this week as "a mess".

As for Project Stormfury, it is being "suspended" because NOAA does not have enough suitably equipped planes. NOAA was planning to move the project from the Atlantic, where it has had dubious success in mitigating the effects of hurricanes by seeding, to the Pacific. The activities of the National Hurricane Research Center will also be scaled down.

The consolidation of earthquake research within USGS is a casualty of President Nixon's cutback on federal expenditure this year, but it must also be acknowledged that there have been many complaints during the past few years that earthquake research is poorly coordinated in the federal government —the latest such complaint came from the General Accounting Office last year. Those who have argued for coordination will be the first to complain, however, if their recommendations are used as excuses for cutbacks.

INTERSTELLAR COMMUNICATION

Eye on the Future

by our Cosmology Correspondent

"We now have the technological capability of mounting an effective search for extraterrestrial intelligent life.". This is the principal conclusion reached by B. M. Oliver after the Project Cyclops summer study programme, funded by NASA, of which he was co-director. The full report of that summer study has now been published, and provides perhaps the most detailed study of the interstellar communication problem now available (copies may be obtained from John Billingham, NASA/Ames Research Center, Code LT, Moffett Field, California 94035).

One-third of this 240-page report deals with the fundamental problem of life in the universe, sets out reasons for attempting communication and determines the most effective means of contact. Not surprisingly, it turns out that electromagnetic radiation is the best tool for the job; the rest of the report, which specifies in considerable detail the antenna system needed, is where this study has the edge over previous work.

The size of instrument which the Cyclops team require is some 3 to 5 km diameter. They suggest that a circular complex of antennae, each 100 metres in diameter, surrounding a control room complex would be suitable for the job, the antennae being linked and phase switched to mimic one giant steerable array. This huge phased microwave antenna would be useful for many purposes; some idea of its power is given by the analogy that it could map Venus by radar as accurately as the Moon is mapped today, or Pluto with the accuracy now available for Mars studies. The advantages to radio astronomy are an obvious fringe benefit. An order of magnitude more powerful than existing arrays, the Cyclops system could also incorporate optical telescopes for simultaneous observation of sources. The sensitivity of Cyclops would be 4×10^6 times that of the late Ozma system (for a detailed comparison of Cyclops and Ozma see table) and could detect signals from thousands of light years away, assuming a plausible power output from the source.

Table 1 Comparison of Ozma and Cyclops Parameters

Parameter	Ozma	Cyclops
Antenna diameter	26 m	3,160 m
Antenna efficiency	0.5	0.8
System noise temperature	350 K	20 K
Resolved bandwidth	100 Hz	0.1 Hz
Integrating time	100 s	10 s
Instantaneous bandwidth	100 Hz	200 MHz

What would all this cost? According to the Cyclops study group, $600 million per annum would allow preliminary planning and site development over 3 years followed by antenna construction at a rate of 100 per year. This compares not unfavourably with large projects such as Concorde, and although vastly greater than any previous scientific budget, is not entirely out of court.

Would the benefits be worth the cost? Certainly, such sums have been spent in the past, and are being spent today, on projects of little or no value to mankind. Even if the assumptions made in the study are completely correct, contact with a superior civilization would be unlikely for decades at least. J. C. G. Walker, writing in this issue of *Nature* (p. 379), is rather less optimistic. Although he agrees that such communication is technologically feasible, he believes that a successful search for extraterrestrial civilizations might require more than a thousand years, even if most habitable planets are occupied by communicative civilizations.

Whether or not such contact is desirable remains largely a philosophical question, and the devotion of some detailed consideration to the use of Cyclops as a research tool could be regarded as an attempt by the team to justify its otherwise abstract project.

Certainly radio astronomy could benefit greatly by being given the funds for an order of magnitude improvement in observation instead of building more instruments comparable with those now in commission. The scale of expenditure suggested for Cyclops, however, runs at four times the total annual expenditure of the British Science Research Council. Perhaps the question is whether it is more efficient or more satisfying to spend $600 million a year asking the stars for, say, a cure for cancer or to spend the same sum on cancer research on Earth.

Short Notes

RIP

An item on page 1 of the January 31 issue of the *New York Times* invited readers to turn to page 38 for an article about how President Nixon is revamping "the entire top echelon of the federal science establishment". Page 38 was, appropriately, the obituaries page. (The article appeared on page 42.)

Kennedy Bill

Some members of the Administration believe that the recent reorganization of the White House Policy machinery may have pulled the rug from under Senator Kennedy's National Science Policy and Priorities Act (S32). The first part of Kennedy's bill calls for the National Science Foundation to be given broader powers in formulating US science policy, and that, of course, is a central part of the reorganization plan announced last week. They also believe that the last part of the bill, calling for retraining programmes for unemployed scientists and engineers, will lose some political appeal if the projected improvement in the unemployment situation materializes. Discussion of the bill would then boil down to its provision for increasing the applied research and development activities of the National Science Foundation. But Congressional supporters of the legislation do not see it that way. For one thing, the bill's statement of objectives would require expenditures on civilian science to increase until they at least reach parity with expenditures on military science, and thereafter to grow at the same rate as the gross national product; the Administration's budget holds out little hope of such growth.

NEWS AND VIEWS

Explaining the Deuterium in the Universe

THE recent detection of deuterium in the Orion Nebula and near the galactic centre has stimulated the interest of astronomers in the processes by which this isotope is produced. Previously the presence of deuterium was definitely established only in the solar system; other measurements merely gave upper limits. Now it seems that the abundance of deuterium relative to hydrogen near the galactic centre is comparable with the terrestrial values, and an even higher deuterium abundance is deduced from the relative strengths of HCN and DCN lines in the Orion Nebula. It is conceivable that some fractionation of D and H occurs in molecule formation, in which case it is not impossible that the terrestrial value, $D/H \sim 10^{-4}$, is fairly widespread in the Galaxy.

Astronomers study the chemical composition of objects in the Galaxy with the hope of discovering to what extent their composition is characteristic of the Galaxy at birth and to what extent it is determined by nuclear reactions which have occurred during the galactic lifetime. It is known that nuclear reactions in stars gradually change the chemical composition of the stellar material and that, if stars lose mass into the interstellar medium, newly formed stars will have a chemical composition different from that of earlier generations of stars. Normal processes of stellar nucleosynthesis do not, however, produce deuterium, which is very easily destroyed by nuclear reactions at the high temperatures in stellar interiors.

It has been known for some time that a relatively smooth abundance of deuterium in the Galaxy could be explained if the life history of the Universe is correctly described by a Big Bang cosmological theory. According to this theory, in which the Universe was initially very hot and very dense and subsequently expanded and cooled, the chemical composition after the initial stages was essentially a mixture of hydrogen and helium and a very small amount of deuterium. The theory also predicts that the Universe should now be filled with microwave radiation which is a highly redshifted relic of the radiation present in the hot early stages of the expansion. The discovery of a cosmic microwave background with a temperature of 2.7 K stimulated interest in the Big Bang theory, which further predicts a relation between the present mean density of the Universe, the microwave temperature and the proportion of helium produced. Although the present mean density of the Universe is not known accurately, all expected values give an initial helium production which is approximately in agreement with observations. By contrast, a deuterium abundance comparable with the terrestrial value is only obtained for the lowest allowable values of the mean density of the Universe; for higher values less deuterium is produced.

If there proves to be a deuterium abundance throughout the Galaxy which is comparable with the terrestrial abundance, the simplest explanation is that the deuterium was produced in a Big Bang. It is not quite as simple as this, for some deuterium must have been destroyed in matter that has passed through stars, but, given a model of galactic evolution, it should be possible to allow for this destruction. Even if it is plausible that the deuterium is primaeval, it is nevertheless necessary to ask whether there are any other processes that could produce a substantial amount of deuterium during the galactic lifetime.

There are two reasons for asking this question. The first is the obvious one that, if there are production processes as well as the destruction mechanisms just mentioned, they must both be studied along with the primaeval abundance in trying to understand the present observations. The second reason is that, although a Big Bang theory is capable of explaining the observed deuterium abundance, one is hesitant to believe that the mean density of the Universe is as low as this would require. To obtain the required primaeval helium abundance almost all the matter in the Universe has to be the matter which is known to be contained in galaxies, so that the intergalactic medium must be essentially non-existent. Although there is still no sure detection of a general intergalactic medium there are several pointers to its existence. For example, attempts to understand the formation of galaxies are much more difficult if it is demanded that most of the matter in the Universe went into galaxies than if the intergalactic medium is still the principal form of mass in the Universe.

For these reasons, Hoyle and Fowler consider on page 384 of this issue of *Nature* whether substantial amounts of deuterium can have been produced in the galactic lifetime. Although deuterium is destroyed efficiently by thermonuclear reactions inside stars, there is one obvious way in which it can be produced. This is by breakdown or spallation nuclear reactions in which α particles are hit by fast protons moving at a significant fraction of the speed of light. Various authors, including Hoyle and Fowler, have previously suggested that, as a result of such reactions during the formation of the solar system, the terrestrial value of D/H might be higher than the initial value for the solar system. Hoyle and Fowler now suggest that these spallation reactions may have occurred in outgoing shock waves from a supernova explosion, or as the result of the explosion of a more massive object, and they estimate that there may have been sufficient explosions to give a general galactic abundance of deuterium comparable with the abundance in the solar system.

It is clear that much more work needs to be done before the relative importance of primaeval and galactic production of deuterium is certain. It is also obvious that there will be continued interest in the subject that Hoyle and Fowler have previously named "deuteronomy".—R. J. T.

Modulation of Transmitter Release

ALTHOUGH it is clear that intercellular communication in the nervous system generally involves the release of chemical transmitter substances from nerve terminals, the mechanisms which may exist for modulating the process of chemical transmission are still obscure. In the past two years, however, several findings have been reported which suggest how the amount of transmitter release at nerve terminals in response to the arrival of nerve impulses may be regulated by the state of ongoing activity at such terminals. In particular, two mechanisms have been proposed to account for the fall-off in the release of noradrenaline from adrenergic nerve terminals during periods of repetitive stimulation.

The first of these mechanisms, proposed by Hedqvist (*Acta Physiol. Scand.* Suppl., 345; 1970), suggests that the release of noradrenaline is controlled by a negative feedback system which involves a local synthesis of prostaglandin E. Sympathetic nerve stimulation or the addition of exogenous noradrenaline has been shown to stimulate the production and release of prostaglandin E from various adrenergically innervated tissues. Furthermore, the exposure of these tissues to exogenous prostaglandin E severely depresses noradrenaline release from the adrenergic terminals, whereas the addition of drugs known to inhibit prostaglandin E synthesis enhances the neurally evoked release of noradrenaline.

A second feedback mechanism, supported by several recent findings (Enero *et al.*, *Brit. J. Pharmacol.*, **44**, 672 ; 1972 ; N. S. Starke, *Archiv. Pharmacol.*, **274**, 18 ; 1972), suggests that noradrenaline may inhibit its own release by an action on α-adrenergic receptors, probably located on the surface of the presynaptic adrenergic terminals. This suggestion is supported by the finding that a variety of α-adrenergic receptor stimulating drugs depress the release of noradrenaline from adrenergic terminals in the heart and other tissues. Conversely, α-adrenergic receptor blocking drugs, such as phenoxybenzamine or phentolamine, enhance the release of noradrenaline from sympathetic terminals in response to nerve stimulation. Both proposed mechanisms thus suggest that the release of noradrenaline from adrenergic terminals is a self-limiting process, which is controlled by local negative feedback mechanisms. Whether those mechanisms are independent, or coupled parts of a single control system, however, has not been clear.

Two new reports throw new light on these problems. Stjärne (*Nature New Biology*, **241**, 190 ; 1973) puts forward evidence which suggests that both of the braking mechanisms described earlier may co-exist in the adrenergic terminals of guinea-pig vas deferens. He studied the stimulus-evoked release of radioactivity from the adrenergic terminals of the isolated vas deferens prelabelled by exposure to radioactive noradrenaline and found that the addition of an inhibitor of prostaglandin synthesis enhances noradrenaline release, whereas low concentrations of prostaglandin E inhibit release. Addition of the α-receptor blocking agent phentolamine, however, after inhibition of prostaglandin synthesis causes a further large increase in noradrenaline release: this suggests the removal of a second braking system capable of operating even when prostaglandin synthesis is inhibited. The α-receptor stimulating drug methoxamine can also inhibit noradrenaline release, after inhibition of prostaglandin synthesis. These results suggest that noradrenaline release, at least from the terminals in guinea-pig vas deferens, is controlled by two different braking systems. Furthermore, these systems do not seem to be interrelated, but to be mediated by different basic mechanisms.

The findings reported by Szerb and Somogyi (*Nature New Biology*, **241**, 121 ; 1973), furthermore, suggest that an "auto-inhibition" mechanism for modulating the amount of transmitter released from nerve terminals may also exist in cholinergic neurones. These authors monitored the release of acetylcholine from slices of rat cerebral cortex exposed to electrical field stimulation, by measuring the outflow of radioactivity from slices preloaded by incubation with tritium-labelled choline. With this recently developed technique acetylcholine release from cortical slices can be measured *in vitro* in the absence of a cholinesterase inhibitor, usually added to prevent the hydrolysis of released acetylcholine. Szerb and Somogyi found that the evoked release of acetylcholine from such slices is inhibited by the addition of an inhibitor of acetylcholinesterase, and a similar inhibi-

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Beetles and Archaeology

BEETLES, it seems, can tell one more about ecological conditions in late glacial and post-glacial times than any other group of fossil land animals, and their Quaternary fossil record can be linked very closely with ecological and distributional knowledge of the species today. This was first clearly demonstrated in Britain through the pioneer researches of G. R. Coope, R. G. Pearson and others. Recent archaeological investigations of a site near Doncaster (see page 405 of this issue of *Nature*) indicate that Bronze Age men of about 1,100 BC made extensive clearances in a major oak forest, in which occurred a number of species of beetles no longer part of the British fauna.

These findings of Buckland and Kenward give some hint of the extent to which the original forest fauna of post-glacial Britain has been impoverished through human clearances and exploitation of lowland woods. Such fragments as still remain of deciduous woods, for example, in parts of the New Forest and of Sherwood Forest, are themselves gravely threatened with further faunal impoverishment—there is not one nature reserve in the Sherwood Forest area, and even Denny Wood in the New Forest, which is a nature reserve, has recently been subject to considerable felling in the service of interests other than those of nature conservation. Many more species of woodland beetles, which might provide valuable archaeological evidence, are in imminent danger of extinction in such places.

—From a Correspondent.

tion of release is produced by adding oxotremorine, a stimulant of cholinergic muscarinic receptors. The inhibition of acetylcholine release in either case is abolished by the cholinergic muscarinic receptor antagonist drug atropine, which by itself does not alter acetylcholine release. The authors suggest that acetylcholine may act to inhibit its own release by way of muscarinic receptors, and that several previous reports that atropine can cause a stimulation of acetylcholine release can probably be explained by the fact that cholinesterase inhibitors were used in these experiments. In such conditions the high concentration of acetylcholine accumulating in the extracellular space may have caused an artefactual inhibition of transmitter release.

There have been many reports that the rate of release or turnover of the monoamine transmitters noradrenaline, dopamine and 5-hydroxytryptamine in the mammalian central nervous system is generally lower in response to the administration of receptor stimulating drugs and increases in response to receptor blocking drugs. Such findings have been described by the generic term "receptor feedback", and have generally been interpreted in terms of complex polysynaptic reflex pathways. The present findings suggest that some of these phenomena may bear re-examination in the light of the possible existence of local "auto-inhibition" or "prostaglandin" feedback controls at the various different types of presynaptic terminal.—From our Neuropharmacology Correspondent.

Gamma-ray Statistics

ONE needs a certain grim determination to be a gamma-ray astronomer these days. It is now fourteen years since experimentalists were fired with enthusiasm by a paper by Morrison (*Nuovo Cim.*, **7**, 858 ; 1958) which stressed the importance of making astronomical observations in the gamma-ray region of the spectrum ; but, in spite of the expenditure of a great deal of money and effort, there have been very few discoveries in gamma-ray astronomy.

The potential importance of this branch of astronomy is easy to understand. Observations in radio astronomy have shown that many regions of the Universe contain large fluxes of very energetic particles. The physical conditions in these regions are still poorly understood, but there is little doubt that the energetic particles should produce gamma-rays in interactions with matter, with radiation and with magnetic fields. Understanding of these regions should, therefore, benefit greatly from observations in the gamma-ray part of the spectrum.

Several basic experimental problems have hindered the development of gamma-ray astronomy. The Earth's atmosphere strongly absorbs all but the highest energy gamma-rays and the measurements must be made from high altitude balloons or from satellites. There is also a large background flux of gamma-rays produced in interactions of cosmic-ray particles with the Earth's atmosphere or with the detector itself. Finally, the flux of gamma-rays which can be expected from even the strongest sources is very small. This means that statistical fluctuations seriously limit the sensitivity of detectors.

The development of the spark chamber in the 1960s gave a fresh impetus to gamma-ray astronomy. At energies greater than 10 MeV gamma-rays interact with a detector through the process of pair production, and the direction of the electron-positron pair—and hence the direction of the gamma-ray—can be measured accurately in a spark chamber. During the 1960s, larger and larger spark chambers were built for experiments on high altitude balloons ; the biggest now has an area of 2,500 cm^2 and the balloons provide exposure times of the order of a day. In 1972 the SAS-B satellite, containing a spark chamber with a collecting area of 225 cm^2, was launched.

An alternative experimental approach is possible for gamma-rays with energies greater than 10^6 MeV. When a gamma-ray of this energy interacts with the Earth's atmosphere it creates an electromagnetic cascade of electrons, positrons and gamma-rays. The electrons and positrons produce Čerenkov radiation in the atmosphere, and this reaches the ground as a pool of light several hundred metres in diameter. This light can be detected, and its direction can be measured by means of a photomultiplier at a focus of a concave mirror. The effective area of this detecting system is the area of the pool of Čerenkov light, which is very much larger than the area of the mirror, and this helps to compensate for the very low number of gamma-rays which can be expected at these energies. This technique has been fully exploited by the group at the Smithsonian Observatory, led by Fazio and Weekes, which has constructed a concave reflecting system 10 m in diameter at Mt Hopkins, Arizona.

The results of all this experimental effort have been disappointing. It was soon realized that the early theoretical predictions were far too optimistic ; in fact, gamma-ray astronomers still do not know how sensitive their detectors should be if they are to develop this branch of astronomy. Of course, the past fourteen years have not been uneventful. Whenever any band of faithful devotees search doggedly for the truth, some will see hallucinations. In gamma-ray astronomy hallucinations take the form of statistical analyses, carelessly applied. One may not agree with Ehrenfest, who is reputed to have told a student, "If you need to use statistics to support your argument, then you are probably wrong anyway" ; but one seems to read too often of results which ". . . have a very low probability of being due to a chance fluctuation" but, eventually, turn out to be just that.

On page 376 of this issue of *Nature* O'Mongain attempts to apply rigorous statistical tests to data published in recent experiments. He concludes that, at an energy of approximately 100 MeV, four sources have been detected —the pulsar in the Crab nebula, two sources in Sagittarius and one in Libra. At energies greater than 10^6 MeV only the Crab pulsar has been detected. No doubt, some experimentalists will disagree with O'Mongain's analysis ; but few will deny that the subject benefits from an occasional critical survey of this kind.

This year will be a crucial one for gamma-ray astronomy. The SAS-B satellite was launched late in 1972 and, apparently, is functioning well. By the end of the year there may well be many more well authenticated sources. The experimental problems will still be severe because astronomy is concerned not only with detecting sources but also with measuring their size and position, measuring spectra and detecting time variations, all of which will require detectors with even greater sensitivities. But when one has cleared Beecher's first time round, the rest of the course looks much less formidable.—R. R. H.

RADIATION

Tissues at Risk

from a Correspondent

SUBJECTS discussed at a meeting held in London on January 9 by the Society for Radiological Protection included malignancies arising from exposure of the bone and lung to radiation and recent data which have led to improved methods of assessing the radiation dose to those tissues from radionuclides deposited therein.

In his account of the origin, structure and radiosensitive areas of the bone, Dr J. F. Loutit (MRC Radiobiology Unit, Harwell) identified haematopoietic marrow, endosteum and cranial epithelia adherent to bone surfaces as the principal sites containing cells with a high proliferative potential and therefore at risk from radiation. He added that malignancies can and do arise elsewhere and cited as an example a high incidence of haemangioendotheliomas—tumours of the walls of the blood vessels—which he had recently observed in mice injected with ^{90}Sr. The induction of tumours is related not only to the chemical behaviour and energy range of the radiation of bone seeking radionuclides but also to half life. Whereas ^{224}Ra with a short 3.8 day half life induces in man chiefly osteosarcomas, ^{226}Ra with a half life of 1,620 years induces both osteo and fibrosarcomas.

The relative radiotoxicities of ^{224}Ra and ^{226}Ra were considered by Dr G. W. Dolphin (National Radiological Protection Board, Harwell) who pointed out that per unit dose averaged over the skeleton, ^{224}Ra, the shorter lived nuclide, induces a greater number of tumours than does ^{226}Ra. One reason for this difference could be that the dose to cells at the bone surface relative to that averaged throughout the skeleton will be greater for ^{224}Ra than ^{226}Ra because the short-lived ^{224}Ra releases much of its α energy at the bone surface and ^{226}Ra most of its α energy after it has become distributed throughout the bone volume.

Methods developed by Professor F. W. Spiers (University of Leeds) for calculating the microdistribution of dose within the tissues of bone were described by Miss J. Whitwell (University of Leeds) and Mr P. Darley (Central Electricity Generating Board, Berkeley). These methods have already assisted greatly in the interpretation of the effects seen from radionuclides deposited in bone.

Dame Janet Vaughan (University of Oxford) identified the haematopoietic marrow as the tissue at greatest risk when the whole body or trunk is exposed to external radiation. The most common malignancy is leukaemia, but, as Dr Vaughan emphasized, the latent period for leukaemia is short relative to that for other neoplasms such as osteosarcoma. These have been observed in groups which have been studied for 10 years or more after exposure. Such people are the ankylosing spondylitics and the children originally irradiated *in utero*. Leukaemia attributed to bomb radiations has been more in evidence in Hiroshima than in Nagasaki. Fast neutrons present in Hiroshima but not in Nagasaki have been incriminated. One effect of localized external irradiation in young children has been the development of exostoses, benign bony outgrowths, rather than osteosarcomas after radiation therapy for enlargement of the thymus.

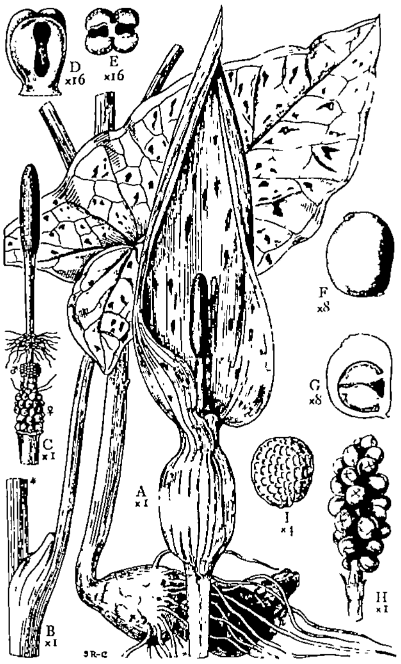
In her review of the structure and metabolism of the lung Professor L. Reid (Institute of Diseases of the Chest, London) described as recent findings the presence of nerve endings in the alveoli and in the epithelium of the airways and the function of the brush borders in regulating the amount of fluid on the surface of the airways. She also defined the areas of deposition of particles of various sizes and also their clearance times. The longest, 60 to 120 days, is the normal clearance time from the alveoli, but this can be increased by tobacco smoke which immobilizes the cilia in the airways.

In spite of difficulties in obtaining relevant information concerning the incidence of radiation-induced lung cancer, Dr S. Rae (National Radiological Protection Board, Harwell) said that it is higher than normal in groups of haematite, fluospar and uranium miners exposed to radon. Cancers are predominantly of small undifferentiated cells in the hilar region of the lung and are more numerous on the right than on the left side. Some of the cancers may be attributable to the daughter products of radon.

Dr J. Vennart (MRC Radiobiology Unit, Harwell) said that the present recommendations of the International Commission on Radiological Protection in respect of maximum permissible concentrations were based on radiation

BRITISH PLANTS

Lords and Ladies



THIS figure shows Stella Ross-Craig's drawing of *Arum maculatum* (commonly known as lords and ladies, cuckoo pint or wake robin) for the thirtieth and penultimate part of her authoritative series *Drawings of British Plants* (Bell, London, 1973). This new section covers the Juncaceae, Typhaceae, Sparganiaceae and Araceae.

Nuclear Steroid-receptor Complex

ENDOCRINOLOGISTS nowadays believe that steroid hormones are transported to the nuclei of target cells by specific cytoplasmic receptors which bind the hormone, presumably at the cell surface, and then migrate to the nucleus. Precisely how the hormone enters the nucleus and there alters the pattern of gene expression remains obscure, but, according to Liang and Tymoczko who write in *Nature New Biology* next week (February 14), the nuclei of prostate and uterine cells contain ribonucleoprotein particles respectively able to associate specifically with androgen and oestrogen-receptor complexes.

Liang and Tymoczko prepared ^{3}H-hormone-receptor complexes from cytoplasmic extracts of rat prostate and calf uterine tissue. They also isolated from the chromatin of the nuclei of these cells ribonucleoprotein particles which sediment at 30S and 80S respectively. *In vitro* these nuclear ribonucleoprotein particles specifically associate with the corresponding ^{3}H-hormone-receptor complexes. After heating or treatment with pancreatic ribonuclease, however, the nuclear particles lose this ability to bind hormone-receptor complex.

Liange and Tymoczko speculate that these nuclear particles may play some part in either effecting the entry of the hormone-receptor complex into the nucleus or mediating the action of the hormone on the genome. Whether these speculations are valid will no doubt emerge as these nuclear ribonucleoprotein particles are further characterized.

dose averaged throughout the whole lung, presumably because the actual sites of critical tissues had not yet been identified. A comprehensive model for deposition and clearance of dust from the airways was now available and could be used to calculate doses in different parts of the respiratory system, for example, to the cells of the bronchial epithelium, which is a possible site for the induction of cancer by radon. It has been suggested that the lymph nodes may not be critical sites because observed malignancies in experimental animals are largely pulmonary. There is a need to identify the radiation sensitive tissues and to examine the ICRP concept of dose commitment which implies that risk is related to the radiation dose integrated over 50 years without allowance for the latent period between induction and manifestation of cancer and for the lifetime of the critical cells.

The practical implications in respect of emergency reference levels of radiation following nuclear emergencies were outlined by Miss P. M. Bryant (National Radiological Protection Board, Harwell). Because of the present greater understanding of both the tissues at risk and the metabolism of radionuclides such as ^{90}Sr there is a possibility that these levels may be increased.

ENTOMOLOGY

Emergence Times

from our Insect Physiology Correspondent

IT has long been known that the eclosion—emergence—of different insects tends to occur at a specific time of the day or night, and that individuals not quite ready to achieve eclosion one day must wait until the same time next day. That was described many years ago by Corbet for emerging dragonflies. In the current lingo an act or process controlled in time by a circadian clock of this kind is termed a "gated event", on the helpful analogy of a gate which is opened only at fixed times of day and for fixed periods. The emergence of *Drosophila* from the pupa is a good example described by Pittendrigh and Skopik in 1970.

There are several examples of the gating process being centred in the brain. That is so in the photoperiodic termination of pupal diapause in *Antheraea* (Williams and Adkisson, 1964). And in this same silk moth, Truman and Riddiford (1970) showed that under the action of the appropriate photoperiod certain neurosecretory cells in the brain liberate an "eclosion hormone" which switches the entire behaviour from pupal to adult type. This includes release of the labial gland secretion which dissolves the silk cocoon, and all the other acts involved in escaping from the old cuticle, expansion of the wings and lysis of the intersegmental muscles. Secretion of the eclosion hormone is evoked by the photoperiod to which the pupa is exposed; but liberation of the hormone at a particular time of day is gated by an inherent circadian rhythm in the brain.

In a recent report Truman (*J. Exp. Biol.*, **57**, 805; 1972) describes a study of the corresponding process of moulting during the larval stages and shows that the timing of the moults is not controlled by a similar mechanism. A direct correlation exists between the time of ecdysis and the time of release of the prothoracotropic hormone (PTTH) from the brain, which does not suggest that ecdysis is controlled by a circadian timing mechanism. The time of ecdysis is sensitive to temperature, which suggests that a developmental process is involved. Moreover the synchrony of ecdysis within a group of larvae is maintained even in larvae ligated at the neck: the head is not needed to trigger ecdysis. In fact, the time of shedding the larval cuticle is determined by a developmental process which requires a fixed number of hours (depending upon temperature) after the gated release of the PTTH from the brain. For this process a longer time is required in *Antheraea* as the larva increases in size; thus each successive ecdysis occurs at a progressively later time of day.

The nature of the stimuli that induce secretion of the PTTH, which acts on the prothoracic gland to cause the release of the moulting hormone, ecdysone, is not known in the case of caterpillars. But once these stimuli have been received the brain releases hormone from the neurosecretory cells only during a specific time of day—the "gating period". Although the timing and duration of these gating periods, during which hormone is released, are more or less independent of temperature, the percentage of the population which is able to exploit a given gate, being dependent on a developmental process, is markedly influenced by temperature. It is interesting to find these two different mechanisms for the timing of ecdysis operating respectively in the caterpillar and in the chrysalis of the same insect.

PROTEINS

Innards *in situ*

from our Molecular Biology Correspondent

SOME interesting new offerings in the current journals concern themselves with aspects of the chemical and conformational constraints that act on a polypeptide segment and its side chains when it forms part of a native globular protein. How, for instance, to assess the effect of a unique environment within a protein on the behaviour of an ionizing group is a problem that has

Reversion of HGPRT$^-$ Cells

MUTANT cells resistant to particular drugs, coupled with cell fusion techniques, are being routinely used today by somatic cell geneticists to produce hybrid cells for genetic analysis. In particular, mutant mouse A9 cells and mouse RAG cells which lack hypoxanthine-guanine phosphoribosyl transferase activity (HGPRT$^-$) and so are resistant to 8-azaguanine have been widely used in fusion experiments with cells lacking thymidine kinase (TK$^-$) activity and are therefore resistant to bromodeoxyuridine. When HGPRT$^-$ cells are fused to TK$^-$ cells the hybrids can be selected by plating in Littlefield's HAT medium in which the parental cells cannot grow but the hybrids survive because of complementation. But, as Shin, Caneva, Schildkraut, Klinger and Siniscalco point out in *Nature New Biology* next week (February 14), this selection procedure rests on the assumption that the mutant parental cells do not revert, and they find, contrary to expectation, that both A9 and RAG mutants do indeed revert from the HGPRT$^-$ phenotype to the HGPRT$^+$ phenotype at a low but significant rate.

Because reversion of these mutant A9 and RAG cells had never been reported, Caneva *et al.* chose them for an attempt to detect transformation of mammalian cells. They exposed A9 and RAG cells to HeLa cell DNA in the presence of inactivated Sendai virus to facilitate uptake of the DNA and they also set up the appropriate control experiments. Much to their surprise mouse cells able to grow in HAT medium and containing HGPRT activity could be selected from both experimental and control experiments.

Moreover, electrophoretic analysis of the HGPRT in these cells revealed that the enzyme was murine, not human. Apparently, therefore, in conditions which promote cell fusion, A9 cells and RAG cells revert at rates of 1.8×10^{-8} and 9.0×10^{-8} respectively. Why this should be the case when the cells do not revert if plated in HAT medium in the absence of Sendai virus and the nature of the genetic changes in the parental "mutant" cells and the revertants are intriguing problems. Clearly these findings have far reaching implications for somatic cell geneticists who are using these particular cells.

long exercised protein chemists. Spectroscopic and chemical methods have been devised, and one of the most successful has recently sprung from the discovery that the C-2 ring proteins of histidine side chains can be resolved in proton magnetic resonance spectra, so that in favourable cases the tritration curves of the individual histidine of a protein can be determined.

An altogether different and potentially very useful approach is given a preliminary airing by Matsuo *et al.* (*J. Biochem., Tokyo*, **72**, 1057 ; 1972), who report as follows: the isotope exchange rate of the C-2 imidazole ring proton can be observed by NMR, and follows the *p*K curve of the ring protonation. Thus a plot of the deuteration rate constant against the *p*H gives the imidazole titration curve. Now at acid *p*H, the rate is evidently infinitesimally slow; thus the exchange rate against tritium can equally well be followed by quenching the reaction at various times with acid, and then determining the degree of titration by scintillation counting. The *p*K of histidine in a tripeptide and of the single histidine residue in lyozyme were determined in this way. After acidifying, the lysozyme solution is passed through a column, and this is followed by acid hydrolysis paper electrophoresis of the product and scintillation counting of the basic amino-acid fraction. Evidently the imidazole side chain is the only one in the protein that retains its tritium through the hydrolysis. The *p*K of his-15 turns out to be *p*H 5.2, whereas in the denatured state it is found to be 7.0. The possibilities will no doubt not be lost on protein chemists, for if this method can be made to work equally well in other situations, and combined with enzymatic hydrolysis and peptide separation, all manner of interesting cases, involving histidines in active sites and the like, could be explored.

The steric accessibility of side chains in proteins is commonly judged by their ability to react with specific reagents. Perham (*Biochem. J.*, **131**, 119 ; 1973) advocates the use of the chromophoric imidoester, methyl picolinimidate, for the determination of available amino-groups in proteins. In TMV protein, the two lysines (53 and 68) react, whereas in the intact virus lys-53 becomes unavailable. In mutants with extra lysines the same situation recurs: a lysine at position 140 remains reactive in the intact virus. In a set of two mutants a lysine at position 9 reacts, whereas one at 33 is reactive in the monomeric protein, but is evidentally engulfed in the structure of the whole virus. There is independent evidence from the position of a heavy-atom label in crystals that position 140 is indeed on the outside of the particle. Position 9 is also expected to occur on the surface, for the first nine residues make up a highly polar segment. At residue 10 hydrophobic character sets in, and the side chains presumably submerge in the structure. In the one mutant it therefore seems as though two out of four lysines, in the intact virus at least, are sequestered. From an energetic viewpoint it should be advantageous if they were to emerge in ion-pair interaction with carboxylate groups. Until comparisons with known X-ray-based structures can be made, the structural implications of anomalous reactivity of side chains must, of course, be approached with caution, as Perham is at pains to stress.

At the conformational level, a new method, minted and burnished in Anfinsen's laboratory, is now on display (Sachs *et al., Proc. US Nat. Acad. Sci.*, **69**, 3790 ; 1972). This depends on the preparation of two kinds of antibodies to a given determinant, or group of determinants, on a protein. One results from immunization with peptide fragments, the other with the whole protein, a specific population of antibodies being

Reiteration of Duck Haemoglobin Genes

In the hands of biochemists reverse transcriptase purified from RNA tumour virus particles has become an invaluable tool for the synthesis of single-stranded DNA complementary to cellular messenger RNAs. The DNA made by reverse transcriptase can be labelled to high specific activities, and for this reason it can be used as a probe for messenger RNAs and their DNA templates in hybridization experiments designed, for example, to measure the expression of a particular gene or the number of copies of that gene per genome. Using this approach Bishop and Rosbash, as they report in *Nature New Biology* next Wednesday (February 14), estimate that in duck cell there may be only two or three copies of haemoglobin genes.

Bishop and Rosbash isolated 10S RNA containing globin messenger from immature duck red blood cells and in the presence of oligo (dT), which acts as a primer for reverse transcriptase, used this RNA as a template for the synthesis of short strands of complementary DNA (cDNA) with a molecular weight of about 1–2×10^5. They then used this cDNA to isolate a cDNA-duck cell DNA duplex. Measurements of the rate of reannealing of cDNA-duck DNA and of duck DNA in the presence and absence of cDNA were then made. From the results of these C_0t analyses, and making allowances for the various problems in interpreting such data, Bishop and Rosbash estimate that the reiteration frequencies of duck haemoglobin genes may be as low as two to three.

This estimate is in close agreement with that reported by Bishop *et al.* last year from data obtained from RNA-DNA hybridization experiments; they concluded that the reiteration frequency of haemoglobin genes in ducks was probably less than five. Such a low degree of reiteration is, of course, in marked contrast to estimates that in sea urchins there may be about 1,200 copies of histone genes.

α Globin mRNA is Lacking in α Thalassaemia

In next Wednesday's *Nature New Biology* (February 14), Grossbard, Terada, Dow and Bank demonstrate that the decreased production of structurally normal α globin chains, typical of α thalassaemia syndromes, can be localized to the level of production of α chain messenger RNA. These workers have investigated the synthesis of α and β globin chains in reticulocytes from non-thalassaemic blood and those from the blood of a patient with haemoglobin H (HbH) disease. The red cells in HbH disease contain a tetramer of four β chains as a result of the relative deficiency of α chain synthesis.

Intact cells from HbH and non-thalassaemic patients were incubated with radioactive leucine, the cells were lysed, globin was prepared and the α and β chains were separated on carboxy-methyl-cellulose (CMC). The ratio of α/β chain synthesis in the intact cells of the patient with HbH disease was 0.55, and the α/β ratio in non-thalassaemic cells was 1.0. Next, mRNA was isolated from HbH and non-thalassaemic blood, and was assayed in a cell-free system from Krebs ascites tumour cells. The products of the cell-free systems were analysed by CMC chromatography and this yielded α/β ratios of 0.79–1.0 for non-thalassaemic cells and 0.13 and 0.17 for HbH cells. The low α/β ratios in HbH blood were not dependent on the concentration of mRNA used.

Thus the decreased production of α globin chains in α thalassaemia is reflected in the chain mRNA associated with polyribosomes. The mRNA in thalassaemic cells, therefore, is either decreased in amount or is abnormal. A similar situation of decreased globin mRNA activity has been reported previously for β thalassaemia.

then absorbed out of the antiserum on a column of a covalently immobilized peptide fragment. This antibody fraction binds specifically to the given peptide fragment, as well as to the intact protein. The differences between the two kinds of antibodies manifest themselves in a number of ways, and the implication is that they are specific respectively for the native and disordered conformations of the antigenic fragment, in this case residues (99–149) of Staphylococcal nuclease. This is the C-terminal part of the chain, and is known from the X-ray structure to be highly α-helical in the native protein, but essentially a random coil in isolation. The native conformation of the nuclease is stabilized by the ligands, calcium and thymidine diphosphate; now whereas these species have only a small stimulatory effect on the precipitin curve of nuclease with native-state antibodies to the single segment, they induce strong inhibition of the interaction with random-state antibodies. Moreover, the former causes inhibition of nucleolytic activity of the enzyme, whereas the other has no such effect.

Contrariwise, interaction of native-state antibody with the free fragment was weak (the binding measurements being made by estimation of uncombined antibody in terms of its inhibitory effect on the activity of added native nuclease). An active enzyme can be made by recombination of N-terminal and C-terminal fragments, but Anfinsen and his colleagues have also found that fragment (6–43) will combine with (50–149) to give what seems to be a conformationally native molecule, with, however, no activity (for which some at least of the missing residues are essential). This, so to speak, emasculated enzyme will combine well with the native-state antibodies. If then one regards the separated fragments of the chain, which, as stated, are more or less random coils, as existing in a state of equilibrium between the random and the folded conformations, in which the former is overwhelmingly favoured, then introduction of the native-state antibody will trap the folded form, and so displace the equilibrium.

From a comparison of the antibody-antigen association constant with the antigen in the folded and unfolded forms (intact protein and free peptide respectively), the conformational equilibrium constant for the peptide fragment can in principle be easily enough determined. Many other well characterized situations involving coupled equilibrium of this kind are known. This approach offers what is probably the only rational basis at present available for some sort of experimental estimate of a conformational equilibrium constant, when the equilibrium favours one form to an immoderate degree.

HUBBLE CONSTANT

New Determination

from a Correspondent

SINCE 1939 when Rudolph Minkowski used the 100-inch telescope on Mount Wilson to obtain slit spectra of supernovae, their interpretation has been a major puzzle to astrophysicists. Minkowski himself described the spectra as being overlapping Doppler-broadened emission lines of unknown origin. Recently, however, the notion originally due to Pskovskii has been gathering support that many, if not all, the spectral features can be explained as very broad absorption lines superposed on a continuous spectrum.

This interpretation has now been applied to Type I supernovae by David Branch and Bruce Patchett of the Royal Greenwich Observatory in the *Monthly Notices of the Royal Astronomical Society* (**161**, 71; 1972). Hitherto the Type I spectra have been the most puzzling of supernovae spectra as they lack even the familiar landmark of the Balmer lines of hydrogen which are present in Type II supernovae. Branch and Patchett show that one can identify nearly all the intensity minima in the spectra of the two supernovae originally studied in the 1930s by Minkowski with lines of singly ionized iron with a blueshift of 10,000 km s^{-1}. Further, they construct synthetic spectra using lines of titanium, scandium, magnesium and silicon as well as iron. These show that, when the excitation state and abundance of each species are considered, the iron lines are indeed most prominent, that several remaining minima in the spectra are explained and that the overall agreement of the observed and synthetic spectra is good.

Branch and Patchett then go on to use their line identifications and the outflow velocity derived therefrom to determine the distance to the supernovae by the first application of a method originally suggested by Leonard Searle of the Hale Observatories. Because by the Stephan-Boltzmann law the luminosity of the supernova is proportional to the product of the area of the star and the fourth power of the effective surface temperature, data on the light and colour variations of the supernova as the outburst proceeds give the fractional rate of increase of radius with time. Fixing the outflow velocity leads therefore to a value for the luminosity and hence distance of the supernovae. Although no light and colour curves exist for the supernovae studied by Minkowski, Type I supernovae are sufficiently homogenous to adopt mean curves for the class which are good enough to give an absolute magnitude $M_v \sim -20.8 \pm 0.8$.

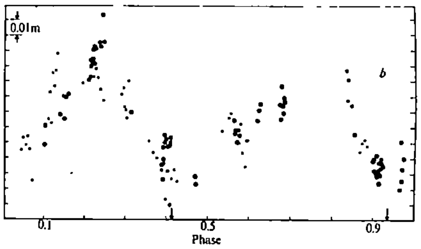
The real importance of this result is that the absolute magnitudes of such distant objects, in galaxies with appreciable cosmological recession velocities and beyond the effect of any local irregularities, provide a new method of determining the Hubble constant. This method is quite independent of the normal astronomical methods which rely on a step-by-step process of distance determination from nearby stars by way of a series of "standard candles" (variable stars, globular clusters, and so on) whereas the method used by Branch and Patchett is, if their model is correct, more directly related to the laws of

Optical Studies of Cyg X-1 (HDE 226868)

THE intriguing system Cyg X-1 is presently receiving attention from X-ray, optical and radio astronomers. The X-ray source was identified with the star HDE 226868 because of the coincidence of a radio outburst from that star with changes in the X-ray flux from Cyg X-1 (see *Nature*, **241**, 246; 1972). The properties of that star have suggested to some astronomers that the X-ray emission must be coming from a black hole orbiting the BO supergiant; but the issue is still open.

In next Monday's *Nature Physical Science* (February 12), Lester, Nolt and Radostitz report photometric monitoring of HDE 226868 (see diagram). These observations do not show the same variability of hydrogen emission which others have reported (see, for example, Bolton, *Nature*, **235**, 271; 1972) and in addition there is now some doubt about whether or not there is an eclipse of the associated X-ray source at all.

Lester *et al.* suggest that the evidence now favours one of two models. First, the companion may not be the source of X-ray emission, or the X-ray emitting region may not be eclipsed; second, the optical data at least are consistent with a tidally distorted binary with no optical eclipse (a possibility also considered by Bolton, *Nature Physical Science*, **240**, 124; 1972). They do not come down on either side of the fence, and it looks as if Cyg X-1 will continue to present a puzzle.



Observations of HD 226868, b′ filter measurements plotted against phase. Arrows indicate conjunction.

physics. It is thus pleasing that their result of $H_0=40^{+25}_{-13}$ km s^{-1} Mpc^{-1} is in good agreement with recent determinations by more traditional methods.

EXOTIC NUCLEI

Limits to Growth

from a Correspondent

THE problem of determining the limits of nuclear stability is one of the great challenges in nuclear physics at present, both from a theoretical and an experimental standpoint. It is, however, a problem that is proving difficult to solve experimentally for all save the lightest nuclei, such as the isotopes of beryllium and boron. It is now known, for example, that ^{12}Be is stable against neutron emission. On the other hand ^{13}Be and ^{14}Be are likely to decay in times of order 10^{-23} s by neutron emission, and cannot be regarded as stable. Recently much effort has been invested in developing a formula which will give the masses of all nuclei in the periodic table, from which the stability of any nucleus can be predicted.

One global approach invokes a liquid drop theory, but for nuclei far from stability the level of accuracy is of the order of several MeV, which is also likely to be the order of the binding energy of neutron-rich nuclei. A more accurate technique uses a stratagem relating the existing mass differences of known nuclei to predict masses of new nuclei to an accuracy of 200 keV. This is the basis of the Garvey-Kelson mass formula, which predicts the stability of such neutron-excessive nuclei as ^{28}O (8 protons, 20 neutrons). Other theories predict the limit at ^{24}O, and it is now the task of experimenters to produce these nuclei in order to make a systematic check on the various theories. Ultimately this problem is of fundamental interest to nuclear physics, because it will be important to see if theories of nuclear structure (such as the shell model) are at all reliable when applied far from the regions of stability in which they were developed.

A dramatic advance in this field was made recently by Klapisch and his group of the Laboratoire Rene Bernas at Orsay (*Phys. Rev. Lett.*, **29**, 1254; 1972); they have produced new isotopes of Na and K. The Garvey-Kelson method predicts that the Na isotope (11 protons) with neutron number between 20 and 28 will be stable if the number of neutrons is even, and marginally unstable if odd. Thus ^{31}Na, ^{33}Na, ^{35}Na and so on should be stable. The Orsay group produced the new isotopes by bombarding uranium with 24 GeV protons from the CERN proton synchrotron. Under this bombardment many nuclear species are produced by spallation reactions, but the alkalis, including isotopes of lithium, sodium and potassium, possess the peculiar and incompletely understood property that they will diffuse out rapidly from the heated graphite which surrounded the uranium target. They can then be transported between the beam bursts of the synchrotron to a detector, shielded by a cadmium enclosure to reduce the intense neutron background. The Na and K ions were selected for transmission to the detector by a simple mass spectrometer. The instrument was first set to detect an abundant isotope ^{22}Na, which has a long half-life, and then the voltage and fields on the spectrometer were accurately adjusted to search for new isotopes. Previous studies using this technique have shown the stability of Na isotopes out to ^{31}Na (11 protons, 20 neutrons). Neutron number 20 is a "magic number" and completes a closed shell. It was possible that the extra binding of the shell closure would mark the limit of stability.

In the new experiment, the stability of ^{32}Na was clearly demonstrated, but the production cross-section was a factor of twenty smaller than for ^{31}Na. This made the task of hunting for ^{33}Na rather difficult, but the researchers were also able to provide conclusive evidence for the stability of this isotope, with a half-life between 5 and 35 ms. The stability of ^{32}Na was unexpected, because it marks a departure from the systematics of the Garvey-Kelson predictions, which seem to be over-pessimistic. The stability of ^{33}Na follows because the added pairing energy of the extra neutron leads to greater binding. It is almost certain that ^{34}Na and ^{36}Na will also turn out to be stable. An exciting possibility is the extension of the technique to study these highly neutron-excessive isotopes, because the decrease in yield from ^{32}Na to ^{33}Na is only a factor of five compared with twenty from ^{31}Na to ^{32}Na. The dramatic drop in yield at neutron number 21 seems to be connected with the closure of the shell at 20 neutrons.

This experimental technique seems to hold the greatest immediate hope for advancing the limit in production of neutron-excessive light nuclei. Ultimately the technique will be able to give precise information on nuclear masses for a more detailed comparison with theoretical predictions. Another exciting possibility is that the method can be applied to a mass measurement of ^{11}Li. This nucleus is known to be stable, but almost every theoretical calculation predicts that it should be unstable to neutron emission by several MeV.

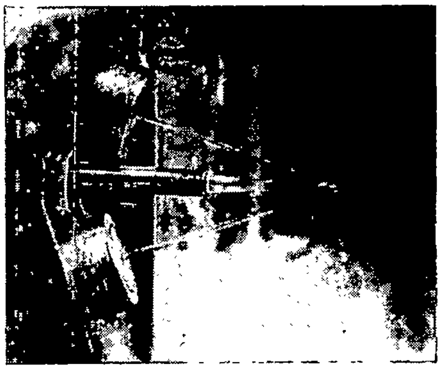
Extensional Viscosity Measured with Three Jets

A NEW way of measuring the extensional viscosity of a liquid (that is the ratio of the time average stress to the extensional strain rate in a jet of the liquid) is reported in next Monday's *Nature Physical Science* (February 12) by Bragg and Oliver. Their apparatus is shown in the diagram; in this so-called "triple jet" system the two outer jets, in which the liquid is travelling at a high velocity, converge on the middle, slower-moving jet and stretch it.

The results and the technique are of particular interest in the context of certain industrial processes, fibre spinning for example, in which stretching flow plays a central part.

Bragg and Oliver were able to obtain extensional strain rates of between 100 and 800 s^{-1}, by comparison with other methods which have either had rather low strain rates (<1 s^{-1}) associated with them, or very high ones ($\sim 10^4$ s^{-1}). In the triple jet method the other component parameter in the extensional viscosity, the time average stress, is deduced by measuring the change in force on the central nozzle as the central jet is stretched.

As expected Bragg and Oliver found that the solutions they used—two aqueous solutions of polyacrylamide and one of 'Polyox'—were very resistant to stretching. Solutions of this type that have shear viscosities of a few cpoise may have extensional viscosities of more than 10 poise: that is the Trouton ratio (of extension viscosity to shear viscosity) is often greater than 1,000. The Trouton ratio is three for a Newtonian fluid.



The triple jet arrangement in operation.

The results show that the extensional viscosity for the three solutions tested goes up slowly with strain rate. The 'Polyox' solutions seem to behave quite differently from the polyacrylamide solutions; the former have higher Trouton ratios at lower extensional strain rates. Thus at 488 s^{-1} the Trouton ratio for 0.1 per cent polyacrylamide solution is 284, whereas at 131 s^{-1} the value for 0.1 per cent 'Polyox' solution is 760.

The Eruption on Heimaey, Iceland

S. THORARINSSON, S. STEINTHÓRSSON,
TH. EINARSSON, H. KRISTMANNSDÓTTIR &
N. OSKARSSON

Science Institute, Division of Geosciences, University of Iceland

Members of the University of Iceland describe the recent volcanic activity in Iceland and present analyses of some of the samples recovered.

On May 5, 1967, the Surtsey eruption came to an end, having then lasted, with short intervals of quiescence, three and a half years. Nearly six years later, on January 23, 1973, a new eruption started in the Vestmannaeyjar archipelago, this time on the biggest island, Heimaey. On that island (see Fig. 1) is situated the town of Vestmannaeyjar; it has 5,300 inhabitants and is Iceland's most important fishing centre.

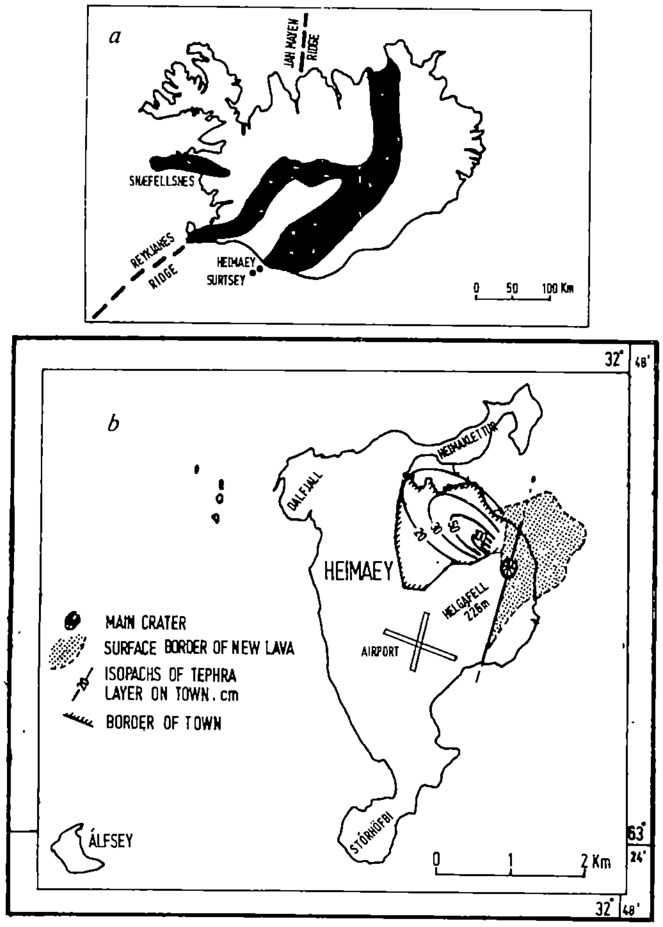


Fig. 1 *a*, The neovolcanic areas of Iceland; *b*, the eruption on Heimaey—preliminary map of the situation after five days of activity.

Precursory Symptoms

Between 2200 h GMT on January 21 and noon the following day many small earthquakes were registered by seismographs situated on the mainland of Iceland. None was felt by people on Heimaey. The foci seemed to be south of Heimaey. At 2230 h on January 22, tremors started again and at least three shocks were felt by people in the town of Vestmannaeyjar. They were more shallow and their foci were on Heimaey.

Eruption Begins

Between 0150 and 0155 h on January 23 a fissure began to open up on the east side of the island of Heimaey. About 5 min before the eruption started there were no signs of eruption here. Within a few minutes of the beginning of the eruption lava fountains were playing on a fissure 300 to 400 m long, and when the photograph in Fig. 2 was taken at 0438 h the length of the fissure was about 1,500 m. It was glowing along its entire length and the height of the glowing fountains was 50 to 150 m. The direction of the fissure is north-north-east to south-south-west.

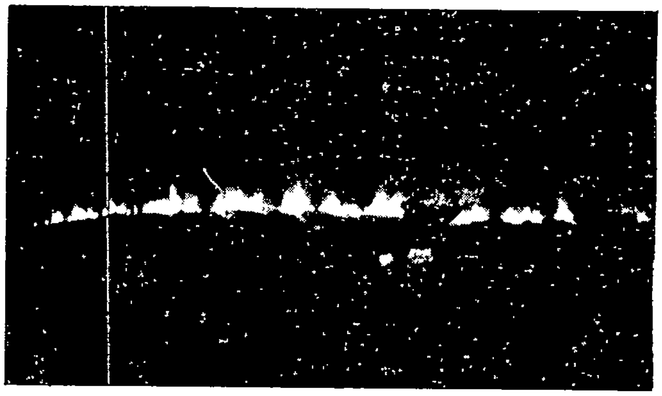


Fig. 2 The lava fissure viewed from the east at 0438 h on January 23. Length of fissure about 1,500 m. The two bright spots beneath the fissure are the two principal lava streams falling over a cliff into the sea.

As the most north-north-easterly part of the fissure runs only 200 to 300 m from the easternmost part of the town, evacuation of the inhabitants started immediately and within 4 h all inhabitants, except a few hundred who had to stay at their posts, had been evacuated without any casualties, chiefly by the fishing fleet which happened to be in the harbour but also by planes sent from the airports at Reykjavík and Keflavík. Because of its close vicinity to the eruption the town was threatened by tephra fall, principally glowing bombs, and by lava flow, the chief threat of which was that it would block the harbour. Fortunately the lava flowed principally towards the east and during the first few days the wind blew the tephra cloud away from the town. But during the night of January 26, wind from the south-east blew the tephra over the town for 8 h. This happened again on January 27, between 1500 h and 0100 h the following night, and the isopachs on Fig. 1 show the thickness of the tephra layer in town after the latter tephra fall had ceased. Repeated south-easterly winds have now added to the thickness and on January 29 the thickness of the layer varied from 30 cm in the north-west part of the town to more than 5 m in the south-east part; between 50 and 100 houses have either been burnt down, chiefly by glowing bombs falling through windows, or buried by tephra, or they have collapsed because of the tephra load on their roofs. The windows facing the eruptions in the southern part of the town have now been covered with sheets of corrugated iron and this has greatly reduced the risk of house fires.

Continuing Activity

At 1030 h on January 23, the north-north-east end of the fissure had extended 150 to 300 m into the sea and small cock's-tail explosions built up a tiny island, which was soon reached and covered by the advancing lava. At noon on the same day the activity had nearly ceased in the southernmost third of the fissure and the fountain activity was beginning to concentrate in the middle of the fissure, where it had first opened up.

After five days of activity the lava flow (see Fig. 1) covered 1.35 km^2 and its volume was roughly 35 million m^3, corresponding to an average flow of about 80 $m^3 s^{-1}$. The flow during the first few days probably exceeded 100 $m^3 s^{-1}$. The eruption column occasionally rose to 9,000 m, or nearly to the tropopause. The relative height of the principal tephra cone which formed around the active part of the fissure was about 100 m on January 27, and had increased to about 150 m (absolute height 180 m) by January 30.

On the morning of January 25, a short submarine ridge was built up to a height of about 10 m on the continuation of the fissure towards the north-north-east, nearly 1 km from its end. At the same time the fissure was extended about 300 m into the sea towards the south-south-west (Fig. 1), thus reaching a total length of nearly 3 km. Some explosions were observed at that end of the fissure, but since noon that day no submarine activity has been observed. Between January 26 and 30 the eruption slowed down considerably.

Ground Water Temperature

In 1964 a drillhole 1,565 m deep was sunk by the National Energy Authority at the west end of the harbour, some 2 km from the fissure. The day after the eruption started the water level in the hole had risen by 10 m, and the temperature at a depth of 800 m had increased by 10° C. Further developments are being monitored by the Energy Authority.

Chemistry and Petrography

Six new chemical analyses are reported in Table 1. The composition of the new rocks is intermediate between those Snaefellsnes rocks termed hawaiite and mugearite by Sigurdsson[1]. They belong to the alkali basalt-trachyte suite. The analyses represent four specimens from the first two days of the present eruption, and two from older formations on Heimaey. The samples were selected partly to test variation with rate and environment of cooling. One represents a lava flow, two are bombs, and one is a tephra. The chief difference between the four is, as to be expected, in the oxidation state of the iron; this aspect will be discussed later in this article.

Fluorine and chlorine were analysed in the leachate from the scoraceous surface of sample 2 (No. 2a, see Table 2), resulting in 100 p.p.m. F and 190 p.p.m. Cl. Two of us (N. O. and S. S., to be published) found, first, that comparable samples from the Hekla eruption of 1970 contained 375 p.p.m. F and 200 p.p.m. Cl, and, second, that these elements are confined to the surface of the ejecta. Hence their concentration varies inversely with the grain size of the tephra. Thus, the Hekla tephra contained 1,000 p.p.m. F and 1,400 p.p.m. Cl at a distance of 170 km from the volcano.

Modal analyses of four samples representing different rates of cooling are shown in Table 3. Sample 8 is from a bomb ejected from the subaqueous crater at the northern end of the fissure. The bomb was chilled in the sea. The modes, however, indicate but a minor increase in crystallization from the chilled sample to a lava. The bomb is highly vesicular, and optical examination reveals that the crystals were present in the melt before vesiculation, for feldspar laths may be seen protruding into vesicles and sidling alongside them. An inevitable conclusion is that the magma contained some 47% of crystals at the time of eruption. This is in agreement with the high viscosity observed, and the rather low temperatures measured so far in the molten Heimaey lava (1,030° C by comparison with 1,140° C in Surtsey[2]).

Table 1 New Chemical Analyses and Norms of Six Samples from Heimaey

Sample	1	2	3	4	5	6
SiO_2	50.29	49.98	50.19	49.99	46.40	47.75
Al_2O_3	16.77	16.96	17.45	17.26	14.31	16.45
TiO_2	2.58	2.53	2.32	2.40	1.65	3.16
Fe_2O_3	2.15	2.14	1.55	1.17	1.77	2.33
FeO	10.57	10.64	11.07	11.36	10.21	10.93
MnO	0.34	0.33	0.34	0.33	0.22	0.28
MgO	3.22	3.18	3.08	3.12	10.61	4.75
CaO	6.99	7.07	7.08	7.18	11.75	8.84
Na_2O	4.95	4.88	4.84	4.89	2.49	4.05
K_2O	1.30	1.35	1.29	1.36	0.32	0.86
P_2O_5	0.71	0.68	0.62	0.70	0.17	0.42
H_2O^+	0.12	0.04	0.02	0.02	0.05	0.03
H_2O^-	0.05	—	—	—	0.05	0.07
Sum	100.04	99.78	99.85	99.78	100.00	99.92
CIPW norm						
QZ	0.00	0.00	0.00	0.00	0.00	0.00
OR	7.68	7.97	7.62	8.03	1.89	5.08
AB	39.54	38.14	37.93	36.49	16.50	30.52
AN	19.69	20.38	22.07	21.12	26.92	24.16
LC	0.00	0.00	0.00	0.00	0.00	0.00
NE	1.26	1.70	1.63	2.64	2.47	2.02
CO	0.00	0.00	0.00	0.00	0.00	0.00
WO	4.50	4.45	3.91	4.32	12.67	7.18
EN	1.67	1.62	1.31	1.42	7.65	3.33
FS	2.91	2.92	2.72	3.03	4.33	3.78
EN	0.00	0.00	0.00	0.00	0.00	0.00
FS	0.00	0.00	0.00	0.00	0.00	0.00
FO	4.42	4.38	4.42	4.42	13.08	5.92
FA	8.57	8.72	10.14	10.44	8.21	7.46
MT	3.11	3.10	2.24	1.69	2.56	3.37
IM	4.90	4.80	4.40	4.55	3.13	6.00
HM	0.00	0.00	0.00	0.00	0.00	0.00
AP	1.55	1.49	1.35	1.53	0.37	0.92
RT	0.00	0.00	0.00	0.00	0.00	0.00
Water	0.16	0.03	0.01	0.01	0.09	0.09
	100.02	99.76	99.83	99.76	99.93	99.89

Analyst: Science Institute, Division of Geosciences, University of Iceland.

For explanation of sample numbers see Table 2.

The refractive index of the glassy groundmass was measured in four samples. In samples 1 and 2 $n_{glass} = 1.572$; in tephra erupted on January 23 at the south end of the fissure $n_g = 1.568$, and in tephra erupted on January 24 at the north end of the fissure $n_g = 1.575$. Clearly, in view of the advanced degree of crystallization even of chilled samples the refractive indices should not relate to the chemical analyses.

The minerals present are plagioclase, olivine and titanomagnetite. Titanomagnetite was the first phase to crystallize. It occurs as inclusions in both the other minerals, and forms skeletal microphenocrysts about 0.05 mm across. Curie-point analyses on unoxidized samples give $T_C=80°$ C, corresponding to 70% of ulvöspinel in the titanomagnetite.

Table 2 Glossary of Samples Described

Sample No.	Sample description	Collected by
1	Tephra erupted 0400 h, January 23, 1973	S. Jakobsson; January 23, 1973
2	Core of lava spatter erupted 1100 h, January 23, 1973	S. Steinthórsson; January 23, 1973
2a	Margin of same	S. Steinthórsson; January 23, 1973
3	Bomb erupted 1100 h, January 23, 1973 (VE 110)	S. Jakobsson; January 23, 1973
4	Lava at southern end of fissure, flowed January 24, 1973 (VE 111)	S. Jakobsson; January 24, 1973
5	Prehistoric lava from Stórhöfdi, Heimaey (VE 61)	S. Jakobsson; 1966, 1967
6	Volcanic plug, Dalfjall, Heimaey (VE 93)	S. Jakobsson; 1966, 1967
7	Lava from south end of fissure, flowed January 23, 1973	H. Kristmannsdóttir; January 24, 1973
8	Centre of bomb ejected from subaqueous crater at north end of fissure 0200 h, January 23, 1973	Th. Einarsson; January 23, 1973
8a	Margin of same	Th. Einarsson; January 23, 1973

The modes in Table 3 seem to indicate that plagioclase crystallized next. The volume of olivine increases from 3.7% in the chilled sample to 6 or 7% in the more crystalline ones, whereas in the same samples the amount of plagioclase only increases from 34 to 36%. The plagioclase forms laths ranging in size from 0.2×0.04 to 0.5×0.1 mm². Larger phenocrysts (some 2 mm across) occur very rarely. One such has been isolated so far and awaits microprobe analysis. The groundmass plagioclase shows somewhat undulatory extinction, but is not distinctly zoned. In sample 7 the composition, as determined with the U-stage, is $An_{45\pm2}$, and in sample 8 compositions range from An_{45} to An_{55}.

Table 3 Modal Analyses (Volume %)

Sample No.	Plagioclase	Olivine	Opaques	Glassy groundmass
3	36.0	7.6	6.0	50.4
4	37.5	5.3	5.8	51.4
7	35.4	6.1	5.4	53.1
8	33.9	3.7	6.3	56.1

Olivine forms euhedral, frequently diamond-shaped crystals, about 0.15×0.1 to 0.35×0.1 mm² in size. Lath-shaped crystals also occur and their size is about 0.15×0.05 mm². Inclusions of glass are very common, and they have roughly the same shape as the host crystal. The $2V_z$ was estimated to be 70°, from which a composition of Fo_{50} to Fo_{60} is deduced.

Cooling and Oxidation

Table 4 Ferric-ferrous Ratios and Curie Temperatures of Some Samples

Sample No.	1	2	2a	3	4	8	8a
Fe_2O_3/FeO	0.203	0.201	0.603	0.140	0.103	0.128	0.232
T_C°C	560	80/560		80/560	80	—	—

On the basis of Curie-point measurements (made by Mr Leó Kristjánsson) of samples 1 to 4 their oxidation states may be divided into three groups: unoxidized lava (No. 4) shows a clear-cut Curie temperature of about 80° C, indicating titanomagnetite rich in ulvöspinel. In this sample microphenocrysts of homogenous titanomagnetite predominate. Tephra (No. 1) has a distinct Curie point at 560° C. This high degree of oxidation must be ascribed to the influence of the atmosphere during cooling. In the volcanic bombs (Nos. 2 and 3) the curve of demagnetization with temperature possesses a shoulder, such that the upper portion extrapolates to about 80 to 100° C on the temperature axis and the lower portion to 560° C. In the bombs the outer rim is oxidized whereas the core is unoxidized. This may be clearly seen in polished samples: near the margin the titanomagnetite microphenocrysts show a high degree of oxidation (oxidation index III) and the groundmass is studded with tiny grains of magnetite. The surface, and the insides of vesicles close to the surface, are characterized by haematite. Within these samples, oxyexsolution of the titanomagnetite microphenocrysts ceases, and the magnetite disappears from the groundmass. Thus, phreatic activity leads to oxidation, and lavas

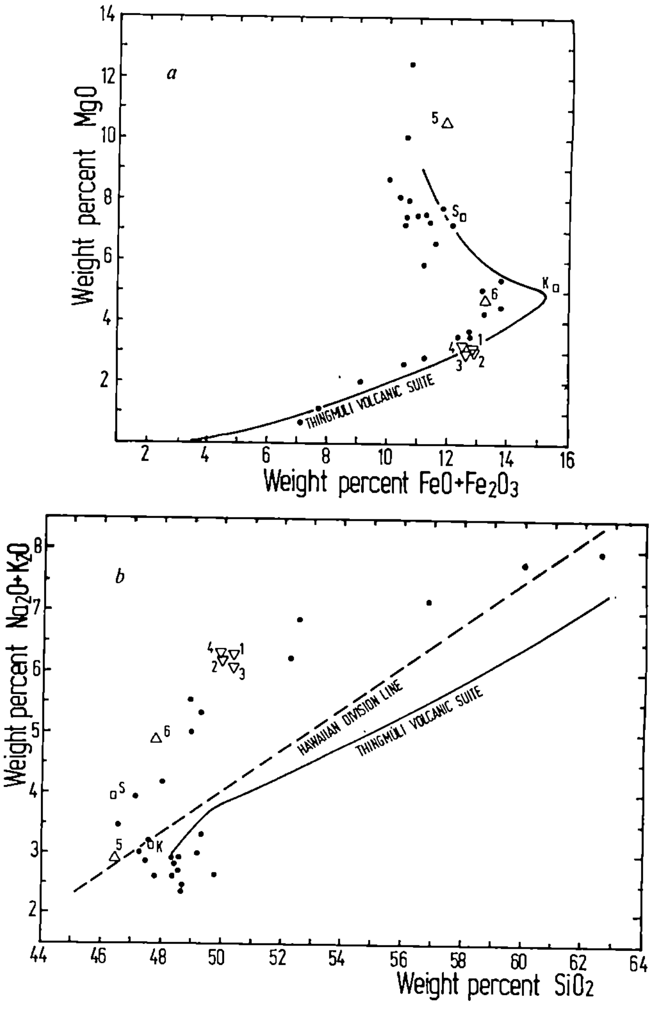


Fig. 3 Analyses of the two alkalic areas. ▽, Heimaey 1973; △, older formations on Heimaey; □, Surtsey 1963 (S) and Katla 1918 (K); ●, postglacial lavas on Snaefellsnes.

should be more oxidized than pahoehoe because of their larger surface area. The rapidity of oxidation may be gauged by the fact that in the water-chilled bomb (No. 8) the outer portion is considerably more oxidized than the core. In Table 4 the ratios Fe_2O_3/FeO of the analysed samples are compared with the Curie temperatures when available. This process of surface oxidation is not to be confused with the increase in oxidation state inwards from crust to core in pillows, dikes and lava flows. The latter phenomenon is a consequence of the buildup of volatiles trapped within the rock, whereas the former is caused by oxidation in the atmosphere.

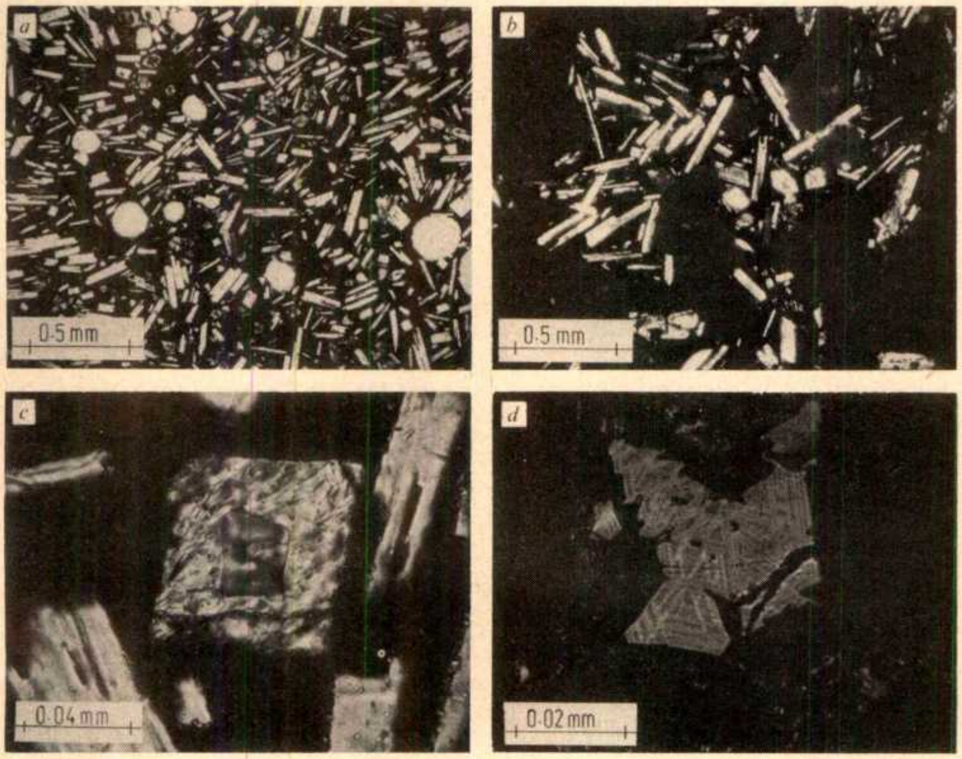


Fig. 4 Photomicrographs of some of the samples. *a*, Lava flow (No. 7). Note alignment of plagioclase laths and inclusions of glass in olivine crystals. (Plane polarized light.) *b*, Chilled bomb (No. 8). Note relationship between plagioclase laths and vesicles. (Crossed nicols.) *c*, Olivine crystal with inclusion of glass. From lava flow No. 7. (Plane polarized light.) *d*, Oxidized titanomagnetite microphenocryst showing trellis exsolution of ilmenite (oxidation index III). From oxidized part of lava spatter (No. 2a). (Reflected plane polarized light; oil immersion).

Photomicrographs of some of the samples are shown in Fig. 4.

Implications

Recent volcanics in Iceland seem to fit into a distinct pattern of distribution[3]. Alkali basalts are confined to the Snaefellsnes peninsula and the south end of the eastern volcanic zone. In particular, the lavas of the central volcano Snaefellsjökull, at the extreme end of the Snaefellsnes peninsula, provide the most complete recent sequence of alkali basalts and their derivatives in Iceland (S. S., to be published). There, the volumes of individual hawaiitic and mugearitic lavas are frequently of the order of 0.1 km³. At the time of writing (January 30) the volume of the new Heimaey rocks is estimated to be about 0.04 km³.

The Vestmannaeyjar region (S. Jakobsson, to be published) shows a more restricted range of compositions. The present Heimaey volcanics are the most differentiated rocks so far analysed from that suite (see Fig. 3 where analyses of the two alkalic areas are plotted). The Thingmuli tholeiitic volcanic suite is shown for comparison[4].

The Snaefellsnes area seems to be all but extinct. The last eruption in that region probably occurred about 1,000 yr ago. Snaefellsjökull itself probably ranges in age from the late Pleistocene to 1,500 or 2,000 yr BP (ref. 5). Conversely, the eastern volcanic zone is now the most active area in Iceland. The greater part of the Vestmannaeyjar islands is thought to have been formed during a relatively short time span about 5,500 yr ago (ref. 6 and S. P. Jakobsson, to be published). This shift in activity from Snaefellsnes to the eastern zone can be related to tectonic changes in Iceland during the past 3 or 4 m.y. (ref. 7 and K. Saemundsson, to be published) in response to westward drift of the North Atlantic system of plates relative to the Icelandic hot spot.

The alkalic areas are situated on the flanks of the actively spreading rift system. The depths of the 2/3 and 3/4 seismic boundaries in Iceland increase away from the Reykjanes zone to the west and east[8] with a concomitant decrease in geothermal gradient[7]. Thus the alkalic provinces may be related to a greater depth of fusion for these rocks, by contrast with the tholeiitic composition of the ridge volcanics[9].

Note added in proof. Microprobe analysis (performed at the Smithsonian Institution, Washington, DC, by courtesy of Dr T. Simkin) has yielded the following results. Bomb ejected on January 23: groundmass plagioclase is $An_{53.6}Ab_{45}$-$Or_{1.38}$ and olivine is $Fo_{61.6}Fa_{38.1}$. Tephra erupted at 1400 h on January 26: plagioclase is $An_{55.2}Ab_{44.8}$ and olivine is $Fo_{63.7}Fa_{36.3}$. Plagioclase and olivine compositions range over 5 and 2%, respectively.

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Application of Statistics to Results in Gamma Ray Astronomy

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Some of the published results in gamma ray astronomy are examined, and it is concluded that not all the sources which have been mentioned can be confidently considered to be present.

THE development of detection techniques in gamma ray astronomy above 1 MeV has begun to yield new and exciting results over more than six decades of energy. The small flux of photons at these energies and the limited collection areas available mean that most of the data consist of small numbers. Observers have usually realized the importance of statistical fluctuations when dealing with these small numbers, so that when there occur positive fluctuations considerably in excess of those expected statistically, it is not unreasonable to ascribe these effects to a "source".

It has already been seen from one set of observations on the Crab Nebula pulsar[1] and the statistical notes it prompted[2,3] that great care must be exercised when expected fluctuations are calculated; full allowances must be made for all degrees of selection imposed on the data. Other apparent effects have appeared[4-6] that have not been verified in later experiments[7-9], although they were deemed statistically unlikely to be chance fluctuations. In this article, a more rigorous application of statistical methods is proposed, along with the use of the relative likelihood function as a source discriminator. The use of the latter function has been described most clearly for these applications by Hearn[10] and by Fichtel *et al.*[11] for upper limit determinations.

The Poisson probability $P(N) = \frac{B^N}{N!}. e^{-B}$ expresses the probability that an event occurs N times in a large group of trials when the average number of occurrences is B, the true average number of occurrences, obtained from an infinite set of trials. The Poisson distribution is discrete, that is, all N are positive integers, and B is a positive number. One often wishes to test whether an experimentally determined number N is likely under two assumptions: (*a*) that the probability distribution of the experimental results is Poissonian, and (*b*) that the mean measured level is indeed equal to B.

Thus, for n sample values of B ($B_1, B_2, B_3, \ldots B_n$) determined experimentally, one should test whether this sample is drawn from some Poisson distribution with an unknown real mean B. The best estimate of B is $B' = \frac{1}{n}\sum_{1}^{n} B_i = \bar{B}_n$, that is, the arithmetic mean (ref. 12, p. 435). The distribution of B_i should be tested by the χ^2 test for agreement with the Poisson distribution (ref. 12, p. 436). Unless this agreement is good, no physical conclusions can be drawn from a single measurement that disagrees with this distribution. Even when the distribution of B_n is found to agree with the Poisson distribution, the value of the mean $B' = \bar{B}_n$ is still only an estimate of the real mean B. The sample size for B' determination should be so large, and the variance of B' so small, that little uncertainty is introduced into any calculations of probability.

In practice, the number of sample measurements of B_i is often so small that (*a*) the uncertainty in the estimate of B is large and (*b*) agreement with Poisson distribution is assumed from experimental experience, rather than tested. Under these circumstances, application of a Poisson probability test must take into account the uncertainty in the estimate of B. Thus, for any single measurement N, a range of possible values of B will exist, with a related range of probability levels.

Even after these tests and allowances have been made, a single experimental determination of N may be found to be highly improbable, for either or both of the following reasons: (*a*) the background level B fluctuated randomly, although this is unlikely for this measurement, or (*b*) an extra source contribution S was present, that is, $N \sim S + B$. Hearn[10] has shown most clearly how the relative likelihood method can be used to determine, at any given confidence level, whether (*b*) is relatively more likely than (*a*). The relative likelihood method can take into account the Poisson nature of the measurements while upper limits, flux confidence levels, and flux errors are obtained in a consistent way. Simultaneously, the sometimes physically unrealistic results of dealing with "standard deviations" can be avoided. Nonetheless, the same limitations apply in this case; the likelihood value is still dependent on a realistic determination of B.

As Hearn has pointed out, the confidence that one can place in any measurement N being the result of a flux S is reduced as the number of attempts to find a large enough value of N increases. Thus, if M bins in the sky are searched for a likely flux S, the confidence one can place in any source found is reduced by a factor M. Equally, for M possible bins in a pulsar-phase analysis, or M possible regroupings of the data, any confidence level is reduced by M. The number M should include all choices of data selection, grouping, regrouping, and reanalysis. It is often very difficult to estimate the number of subjective choices that are made in grouping data; M is only equal to unity when there is only one physically realistic grouping of the data attempted, and only one bin in this grouping in which an effect will be tested for and accepted.

To determine if the results of any search for a gamma ray effect can, in fact, be ascribed with a given degree of certainty to a source, rather than to a statistical fluctuation, one needs to know N, the number of events observed; B, the number of events expected; E_B, the standard error on the estimate of B; and M, the number of attempts made to find N. In the tests that follow, attempts are made to calculate realistic likelihood levels for some of the published gamma ray results; for comparison, Poisson probability levels are also calculated. In many cases, E_B or M are not available in the published results. For these cases, and the others used here, the tests are intended to show only that some of the apparently large fluctuations may not be as improbable as claimed. The tests represent a statistical demonstration rather than a critical analysis of results. I am responsible for any misrepresentation of data that may be present. The results tested are grouped into regions that correspond to those used in ref. 13. Each group of results is analysed by using the formulae and notation of Hearn[10]: these are described in the first group that follows, but the original article should be consulted for complete definitions.

Galactic Centre Region

Table 1 shows the results of tests on observations of the Galactic centre region. For the results of the London group[14], a particular known source position Sgr XR-2 was tested with M assumed equal to 1. Following Hearn, the relative likelihood of the fluctuation observed being due to a source contribution S is

$$L(S) = \frac{P(S/N)}{P(S=0/N)}$$

where the Ps are conditional probabilities. For the case of Poisson probabilities, this simplifies to

$$L(S) = (S/B+1)^N . e^{-S}$$

and the likelihood value L quoted is the maximum value of $L(S)$. The maximum of $L(S)$ is at $S=S_m=N-B$ (for $N \geq B$); $L=L(S_m)$ is the value quoted in the table (or L/M when $M>1$).

At a confidence level C, the maximum likelihood function $L=L(S_m) \geq M/(1-C)$ is used to define a source "discovery", and $L(S_u)/L(S_m)=(1-C)/M$ is used to define the upper limit S_u. In this analysis, $C=0.95$, which corresponds to demanding a 95% confidence level, or a maximum likelihood level of 20. Again, for ref. 14, the error in B could reduce L if the true value of B was in the range B to $B+E_B$. Where E_B is known, the tables show the L value corresponding to $B'=B+E_B$. Where the likelihood value exceeds 20 (confidence exceeds 95%), a source flux and errors are calculated in the manner described by Hearn; $L(S_\pm)=e^{-0.5}$. $L(S_m)$ is solved for S_+ and S_-.

In the testing of the data of ref. 15, $M=960$ has been used; although the authors bunched their bins in 25 (5° × 5°) groups, it appears that they maintained 960 values by using 1° steps. The work of Fichtel *et al.*[16] may have $M>1$, but unless $M \gg 20$, which is unlikely, the result is most probably not a statistical fluctuation. The remainder of Table 1 treats the data of the Case–Melbourne group[17–20]. If one accepts the evidence for Sgr γ-1 in ref. 17, then the data of ref. 18 can be searched at, or near, the location of Sgr γ-1 for a source count—thus M is lowered. The rather large value of M used for Gγ2+3 and Gγ341+1 is deduced from the use of a basic bin size of $1° \times 0.02$ over a region $220° < \alpha < 310°$ and $-59° < \delta < -6°$ (where the 0.02 is in units of sin δ). For the sources Cen γ-1 and Gγ327+2 reported at IAU Symposium No. 55 (ref. 20), the value of M for the number of bins searched is purely my estimate.

Shown in the last column of the table is the Poisson probability P of getting a number N or greater in M observations when the background is $B+E_B$ (or $E_B=0$ if unknown). If p is the probability in one observation, $P=1-(1-p)^M$ is used for M observations or attempts. It can be seen that examining the probability that the effect is a chance occurrence is not the same as testing for the probability or likelihood that the effect is due to a source. One expects 5% of independent tests of data to produce chance effects at the 95% confidence level, but considerably fewer will produce a source likelihood with 95% confidence. In general, source confidence levels obtained by the relative likelihood method in the range 95% to 99.9% will be a factor of 5 to 10 times lower than the corresponding simple Poisson probability "confidence level".

Cygnus–Cassiopeia Region

The data in this and the following groups have been analysed in the manner described for the previous group. Table 2 shows data for some of the results for this region. On the basis of the figures quoted, all the likelihood values are too small to be significant. The apparent source detection by Stepanian *et al.*[7] in the region of Cassiopeia can be examined with normal statistics ($B=1,770 \pm 9.2$, $N=1,940$). This shows a 4.0σ peak in 1 of 21 bins on 3 of 6 nights of observations; thus, $M \sim 126$ and $p \sim 2 \times 10^{-5}$, giving $P \sim 3 \times 10^{-3}$. If this value of $M=126$ includes all degrees of selection, this region should be examined again for confirmation.

Table 3 shows data for the anticentre region. Here, again, there may be no non-statistical effects. The observation on CP 1133 (ref. 27) has not been confirmed by further measurements[5,22,23] and is usually disregarded.

Pulsar Periodicity Searches

Analysis of a phase histogram for pulsar periodicity can be treated in the same way as a sky survey. Either the phase of the pulsar is known exactly and a particular bin can be designated (with $M=1$), or all bins have to be searched. When M bins are regrouped in order to maximize an effect, the number of ways of regrouping multiplied by the number of bins present is still equal to M. The only exception to this is if, in a single purely objective manner, the regrouping is done before any search is made. For the case of the Crab Nebula pulsar, one has to make an objective decision as to whether an effect is sought at the main-peak position, the interpulse position, or both. In the data shown in Table 4, it is assumed that this decision has already been made on some physical basis; if

Table 1 Galactic Centre Region

Reference	Source	Background counts B	Error in B E_B	Observed counts N	Attempts M	Relative likelihood L	Upper limit (counts)	Flux (counts)	Poisson probability P (%)
Bennett *et al.*[14]	Sgr XR-2 2×10^8 eV	34.1	—	48	$\gtrsim 1$	~ 12.3	32.9		1.4
	5×10^8 eV	10.0	—	17	$\gtrsim 1$	~ 7.5	19.2		2.7
	1×10^9 eV	2.5	—	8	$\gtrsim 1$	~ 44.9	—	$5.5^{+3.2}_{-2.6}$	0.42
	2×10^9 eV	1.0	—	2	$\gtrsim 1$	~ 1.5	6.7		26.0
Browning *et al.*[15]	Source No. 1	16	±1.3	29	960	$\gtrsim 0.03$	45.2		99.76
	2	33	±2.6	50	960	$\gtrsim 0.01$	57.9		100.0
	3	22	±1.6	35	960	$\gtrsim 0.01$	47.8		100.0
	4	8	±0.6	19	960	$\gtrsim 0.11$	38.0		100.0
Fichtel *et al.*[16]	Line source	210	—	274	$\gtrsim 1$	$\sim 7.3 \times 10^3$	—	$64^{+16.9}_{-16.3}$	1.4×10^{-3}
Frye *et al.*[17]	Sgr γ-1 Flights I+II	70.1	±1.4	111	200	$\gtrsim 55.9$	—	$40.9^{+10.9}_{-10.2}$	0.18
Frye *et al.*[18]	Gγ2+3 All data	72.6	—	110	~3,330	~ 1.22	94.5		8.29
	Gγ341 All data	68.0	—	101	~3,330	~ 0.32	88.0		30.7
	Sgr γ-1 All data	68.0	—	102	~10	~ 157	—	$34^{+10.5}_{-9.8}$	0.07 0.07
Frye *et al.*[19]	Lib βγ-1 All data	75.0	—	121	100	$\sim 1.4 \times 10^3$	—	$46^{+11.4}_{-10.7}$	6.3×10^{-3}
Frye *et al.*[20]	Cen γ-1 All data	41.0	—	68	(~100)	(16.4)	(64.4)		(0.71)
	Gγ327+2 All data	47.6	—	91	(~100)	(1.5)	(61.5)		(0.91)

any (rather than one) of these three possible effects is to be accepted, M should be increased by 3. The tests are as in the previous tables. In all these results, a measure of E_B is easy to obtain from the phase histogram. All the L values are therefore lower limits. The result from ref. 24 would have an L value greater than 20 if the true background was $\lesssim B$. The final entry shows what a lower energy result[25] looks like when examined in the same way (despite its large M value).

Confidence in the Source Detections

Given the observational parameters B, E_B, N and M as described, it is possible, in general, to provide a reliable and

Table 2 Cygnus–Cassiopeia Region

Reference	Source	Background counts B	Error in B E_B	Observed counts N	Attempts M	Relative likelihood L	Upper limit (counts)	Poisson probability P (%)
Browning *et al.*[6]	Source No. 8	20	±2.0	39	576	$\gtrsim 0.36$	52.6	31.63
	9	7	±0.7	19	576	$\gtrsim 0.61$	37.5	21.49
Niel *et al.*[9]	Apparent No. 1	11.6	—	22	145	~0.27	34.8	44.88
	2	1.7	—	5	145	~0.06	18.2	98.59
	3	15.1	—	24	145	~0.06	34.1	95.39
	4	14.3	—	23	145	~0.06	33.5	95.39
	5	2.8	—	7	145	~0.06	20.6	97.05
	6	10.6	—	17	145	~0.04	28.6	99.82
	7	8.8	—	17	123	~0.16	30.1	66.69
	8	14.7	—	23	123	~0.06	32.8	96.55
	9	11.4	—	20	123	~0.11	31.8	80.00
	10	3.3	—	7	123	~0.04	19.9	99.95
	165–15	57.0	—	81	123	~0.71	65.0	17.88
Niel *et al.*[26]	Cygnus	283	—	325	(~10)	(~2.0)	(104)	(7.53)

Table 3 Galactic Anticentre Region

Reference	Source	Background counts B	Error in B E_B	Observed counts N	Attempts M	Relative likelihood L	Upper limit (counts)	Flux (counts)	Poisson probability P (%)
Forichon *et al.*[21]	66–8	23.1	±2.3	34	144	$\gtrsim 0.03$	37.5		99.99
	65–43	13.5	±1.3	27	144	$\gtrsim 0.39$	38.6		33.22
	70–43	16.4	±1.6	32	144	$\gtrsim 0.56$	42.2		22.85
	76–41	27.5	±2.0	47	144	$\gtrsim 0.56$	50.4		22.85
	82–27	85.5	±3.0	103	144	$\gtrsim 0.02$	60.5		100.00
	83–22	51.5	±2.0	66	144	$\gtrsim 0.03$	52.5		99.97
	96–29	56.4	±2.0	81	144	$\gtrsim 0.34$	64.0		35.12
Frye *et al.*[20]	Per γ-1	56.6	—	91	(100)	(67.1)	(34.4)		(46.31)
O'Mongain *et al.*[27]	CP 1133	81.0	±4.5	122	~4	$\gtrsim 241$	—	$41^{+11.4}_{-10.8}$	0.05

Table 4 Pulsar Periodicity Searches

Reference	Source/energy	Background counts B	Error in B E_B	Observed counts N	Attempts M	Relative likelihood L	Upper limit (counts)	Flux (counts)	Poisson probability P (%)
Frye *et al.*[28]	NP 0532 Main $\lesssim 1.0\times10^7$ eV	27.0	±1.3	47	3	>57	—	$20^{+7.2}_{-6.6}$	0.24
	Main+Inter	54.0	±2.6	75	3	>5.0	48.6		3.26
	Main $>1.0\times10^7$ eV	14.4	±1.0	31	3	>147	—	$16.6^{+6.6}_{-5.3}$	0.09
	Main+Inter	28.8	±2.0	45	3	>5.8	38.2		2.88
Share *et al.*[24]	Main $>1.5\times10^7$ eV	32.0	±1.4	48	1	>16.6	33.6		1.0
	Main+Inter	64.0	±2.8	82	1	>5.0	39.4		3.9
Parlier *et al.*[29]	Main $>2.0\times10^7$ eV	594	±7.0	640	1	>3.5	103		5.9
Browning *et al.*[30]	Main $>5\times10^7$ eV	153	±2.2	180	33	>0.20	77.6		60.8
	Main+Inter	306	±4.4	360	33	>1.3	122		67.0
Frye *et al.*[28]	Main $>5\times10^7$ eV	8.4	±0.7	17	5	>3.1	23.7		5.9
	Main+Inter	16.8	±1.4	29	5	>3.0	30.3		5.9
Vasseur *et al.*[4]	Main $>5\times10^7$ eV	252	±4.6	273	1	>1.7	58.9		16
	Main+Inter	504	±9.2	541	1	>2.1	86.7		12
Grindlay *et al.*[31]	Main $>6\times10^7$ eV	2.73	±0.94*	3	1	—	6.7		71
	Main+Inter	8.19	±2.8	13	1	>2.2	15.7		13
Grindlay *et al.*[32]	Main $>6\times10^{11}$ eV	8.9	±1.4*	13	1	>1.39	15.0		24
	Main+Inter	26.7	±4.2	46	1	>24.6		$19.3^{+7.2}_{-6.5}$	0.66
Porter *et al.*[33]	Main $>2\times10^{12}$ eV	74	±1.7	108	100	>4.36	8.0		2.76
	Main+Inter	148	±3.4	204	100	>37.6	—	$56^{+14.7}_{-14.0}$	0.28
Chatterjee *et al.*[5]	CP 0950 $>1\times10^{13}$ eV	30	±1.0	59	5,000	>4.3	73.9		2.47
Harnden *et al.*[25]	Vela $>2\times10^4$ eV	422	±2.2	550	2,700	$>9.3\times10^3$	—	128±23.8	8.1×10^{-4}

* I have determined E_B from the variance of the data.

consistent measure of confidence in possible source detections in gamma ray astronomy. Once the use of Poissonian statistics can be justified and a good estimate of background count is made, the relative likelihood method can be used to calculate a source likelihood value L. If this exceeds a reasonable value (for example, $L = 20$ for a 95% confidence level), a flux estimate and errors can be calculated; if not, only upper limits can be deduced. It should be noted, as mentioned earlier, that any confidence level C obtained from the L value [$C = 100\ (1 - 1/L)\%$] is lower than the corresponding simple Poissonian "confidence level"; thus, the upper limit obtained by using the relative likelihood function may be larger than many of those already obtained and published.

From the L values obtained here it can be seen that in the Cygnus–Cassiopeia region (Table 2) there is little evidence for gamma ray sources, except perhaps at 10^{12} eV (ref. 7). Even the Poisson probability levels are not impressive. The evidence in the anticentre region (Table 3) is also rather weak. It may take some further time and observations before sources in regions other than at the Galactic centre and the Crab Nebula are accepted by all because of their convincing statistical evidence.

The need for a consistent and reliable statistical test has already been acknowledged; here I have tried to show how statistical tests on results in gamma ray astronomy can show which results are most reasonably ascribed to gamma ray sources. Less significant results can still be exciting and certainly deserve more investigation. If later investigation fails to show an effect, source variability should not be quoted in explanation unless the evidence for the presence of a source is convincing in the first case. It is for such cases in particular that a good estimate of the statistical probabilities or likelihoods involved is needed. The most appropriate test would appear to be the relative-likelihood test described by Hearn[10].

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The Search for Signals from Extraterrestrial Civilizations

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Although the technology exists for exchanging radio messages with extraterrestrial civilizations, a successful search for such civilizations among the many stars that might support them could take more than a thousand years, even if most habitable planets are occupied by communicative civilizations.

THAT the technology exists for sending and receiving radio messages over interstellar distances is not in doubt[1-5] so that, if there are similar technological civilizations based on stars not too distant from the Sun, we can, in principle, communicate with them. A problem, however, is to determine which star out of a large number of candidates is the home of a potentially communicative civilization[6-8]. The subject of this paper is the search problem of interstellar communication.

Occurrence of Habitable Planets

Even the most optimistic estimates of the frequency of occurrence of potentially communicative civilizations suggest that a large number of stars will have to be searched before a civilization is encountered. If we let P_c be the probability that a given star has a communicative civilization, we may write

$$P_c = fP_{HP} \tag{1}$$

where P_{HP} is the probability that the star has a habitable planet in orbit around it, and f is the fraction of habitable planets with communicative civilizations. This fraction involves the probability that a communicative civilization will evolve on a habitable planet as well as the average lifetime of communicative civilizations[6,9–11].

It may be impossible to determine the value of f by other than empirical means, but P_{HP} is a quantity that can, in principle, be estimated from a knowledge of cosmogony and planetology. Dole[12], for example, has made a detailed estimate of the probabilities that planets on which Man could exist are in orbit about stars of different spectral classes. His considerations lead him to conclude that P_{HP} achieves a maximum value of 5.5% for stars of classes G0 to G4, and that 3.7% of stars in classes F2 to K1 have habitable planets; P_{HP} is zero for stars outside this range. Dole's estimates involve many assumptions, and improved values of P_{HP} will undoubtedly become available in time, but his values are adequate for present purposes. They show, first, that several tens of stars must be searched, even if f is of order unity and, second, that we can estimate P_{HP} for different stars and therefore can use this information to guide our search.

Strategy for the Search

One approach to the search problem is to assume that the other civilization will do most of the work, which implies that the search is limited to "supercivilizations" able to transmit detectable signals in all directions all the time[5,13]. We could not do such a thing[14], for the power requirement of an isotropic call signal detectable at a range of 100 light year is approximately equal to the world's present total power consumption[2,15]. We can signal over interstellar distances only by using a large radio telescope to concentrate the radiated energy into a narrow beam. It would be possible to use a number of transmitters to send continuous signals to an equal number of target stars, but for such a strategy to have a reasonable chance of success, the number of transmitters would have to exceed

$$P_c^{-1} = (fP_{HP})^{-1}$$

This number is larger than 18, using Dole's values of P_{HP}, and it may be very much larger, since f may be small.

Even if there were several interstellar transmitters—and there are not—a strategy of continuous transmission to a select group of stars would not, however, be optimal. So as f is unknown, the probability of success for the transmitting civilization is proportional to the number of stars called regularly. In order to call the largest possible number of stars for a given level of effort, transmitter time must be shared among different target stars. How often, then, should a signal be sent to a given star?

Von Hoerner[6] has analysed this problem in general terms, pointing out that it is necessary to develop an optimal search strategy for both transmitter and receiver, and then to assume that the target civilization will perform the same analysis and arrive at the same conclusion. I present here a strategy for which the probability of success can be evaluated, at least as a function of f.

An optimal search strategy should use all the information that we share with the target civilization. This includes the spectral classes of candidate stars and thus the values of P_{HP}; it includes the optimal spectral region in which to work, the region where unavoidable background noise is minimal[1–5] and the distances to the candidate stars.

This last quantity provides the only indication we have as to how often we should look at any given star. The natural repetition period[8] for a star at distance R is

$$T = \frac{2R}{c} \tag{2}$$

where c is the velocity of light. It is the time for a contact signal to travel to the star and for a reply to return. I shall assume that the transmitter sends a contact signal every T years to every star within range having a non-zero P_{HP}. Excess transmitter capacity would be used to increase the range of the search rather than to provide more frequent contact signals.

Although there are a number of ideas about the wavelength to use for contact signals[1,5], a search in frequency cannot be eliminated entirely because extremely narrow bandwidths must be used for interstellar communication[2]. I shall not consider the frequency search explicitly, so for simplicity in the analysis I shall assign this task to the transmitter. Thus the contact signal to be sent out every T years will sweep slowly over the optimal spectral region, and the receiver may confine its search to a single frequency.

Probability of Success

With the transmitter strategy thus defined, it is possible to determine the optimal receiver strategy and evaluate the rate of success. From the point of view of the receiver, let us redefine P_c to be the probability that a given star has a civilization that sends a contact signal to the receiving star every T years at the wavelength on which the receiving civilization is listening. This redefinition introduces a corresponding change in the definition of the unknown fraction f, but no change in the known probability P_{HP}.

If, at the beginning of the search, the receiver devotes a period of time $\Delta\tau$ to listening to a given star, the probability that it will receive a call is

$$P_s = P_c \quad \Delta\tau/T \tag{3}$$

The rate of success in the search is therefore $fP_{HP}/T\ \text{yr}^{-1}$, where P_{HP}/T depends on the spectral class and the distance of the target star and f is the same for all stars. Because the repetition period T increases linearly with distance to the target star, the success rate is highest for the closest stars. Using Dole's figures[17], we find a success rate for α Centauri of $1.3 \times 10^{-2} f\ \text{yr}^{-1}$; for ε Eridani and τ Ceti the success rates are both about $1.5 \times 10^{-3} f\ \text{yr}^{-1}$. For a G0 star at 100 light year, however, the success rate is $2.7 \times 10^{-4} f\ \text{yr}^{-1}$.

But the receiver should not devote all its time to the closest star. This star may not be the home of a communicative civilization. After the receiver has devoted a large number n of randomly spaced listening periods $\Delta\tau$ to a given star, the probability that the receiver will have failed to receive a call, assuming that there is a transmitter associated with that star, is $\exp(-n\Delta\tau/T)$. The probability of success on the next look at the star is therefore

$$P_s(\tau) = fP_{HP}(\Delta\tau/T)\exp(-\tau/T) \tag{4}$$

where $\tau = n\Delta\tau$.

The optimal receiver strategy is now clear. The success rate is maximized if each listening period $\Delta\tau$ is devoted to the star for which $(P_{HP}/T)\exp(-\tau/T)$ is greatest. As the search progresses, the number of stars included in the search increases steadily, for each star within range the value of τ increases, and the instantaneous success rate grows steadily smaller. Each try, however, adds the greatest possible amount to the cumulative probability of success. How much time, on average, must elapse before success is achieved?

Suppose that there are N_i stars of spectral class i per unit volume and let $P_{HP}(i)$ be the probability that each of these stars has a habitable planet. After a total time t has been devoted to the search, following the strategy outlined above, the cumulative probability of success is

$$P_s = \frac{4}{3}\varepsilon f t \tag{5}$$

where ε is the instantaneous success rate at time t given by

Table 1 Search Strategies for Various Distributions of Civilizations

Fraction of habitable planets occupied by communicative civilizations f	Average separation of communicative civilizations (light year)	Duration of search T_0 (yr)
1	24	1.4×10^{3}
10^{-3}	240	1.4×10^{7}
10^{-6}	2,400	1.4×10^{11}

$$\varepsilon=\left[\frac{\pi c^{3}}{32t}\sum_{i} N_i P_{\mathrm{HP}}{}^{4}(i)\right]^{\frac{1}{4}} \qquad (6)$$

From Dole's Table 18, $\sum\limits_i N_i P_{\mathrm{HP}}{}^{4}(i)=1.24\times10^{-9}$ per cubic light year, so

$$\varepsilon=3.3\times10^{-3}\,t^{-\frac{1}{4}}\,\mathrm{yr}^{-1} \qquad (7)$$

and

$$P_{\mathrm{s}}=4.4\times10^{-3}\,f t^{\frac{3}{4}} \qquad (8)$$

where t is expressed in years.

On the average, contact will be achieved when $P_{\mathrm{s}}=1$ or after a search that has lasted

$$t_0=1{,}380 f^{-4/3}\,\mathrm{yr} \qquad (9)$$

Values of t_0 corresponding to several assumed values of f are shown in Table 1. Also shown is the average distance that separates communicative civilizations for these values of f.

We see that even with optimistic assumptions concerning the frequency of occurrence of communicative civilizations, the time required for a successful search is long. Of course, t_0 is, strictly speaking, telescope time devoted to the search, not total elapsed time. The duration of the search is therefore inversely proportional to the number of receiving telescopes and could be shortened by a massive effort. Alternatively, it is possible that the transmitter strategy I have assumed is incorrect, and that more frequent calls would be optimal, say m calls every T years. In this case the duration of the search differs from the values in Table 1 by a factor of $1/m$, provided the receiving civilization knows the value of m.

The conclusion, therefore, is disappointing. If every habitable planet has a communicative civilization there might be 50 such civilizations within 100 light year of us[18]. We possess the technology to exchange messages with this multitude of other worlds, if only we can find them. Unless my assumed transmitter strategy is seriously in error, however, or unless habitable planets are substantially more abundant than Dole has concluded, the problem of finding the other worlds is overwhelming. These circumstances may limit us to a search for supercivilizations[13].

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Correlation between Cultural Characters and Pathogenicity in *Ceratocystis ulmi* from Britain, Europe and America

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Isolates of *C. ulmi* from Britain fall into two groups on the basis of cultural characters. Pathogenicity experiments show one group to be aggressive and the other to be non-aggressive. Some North American isolates resemble the aggressive isolates, while isolates from Northern Europe are non-aggressive.

THE epidemic of Dutch elm disease is continuing to develop in Southern England. A Forestry Commission survey was carried out in September 1971 and it was estimated that 4% of the elm population was dying or dead[1]. By September 1972 the losses had doubled.

There is evidence for the existence of an aggressive strain of *Ceratocystis ulmi* in the worst affected areas[2]. As a preliminary to further investigation of this strain the isolates used in the 1971 inoculation experiment at Alice Holt were examined for variation in culture. Differences between aggressive and non-aggressive isolates were apparent. This phenomenon was examined further by collecting isolates from a variety of

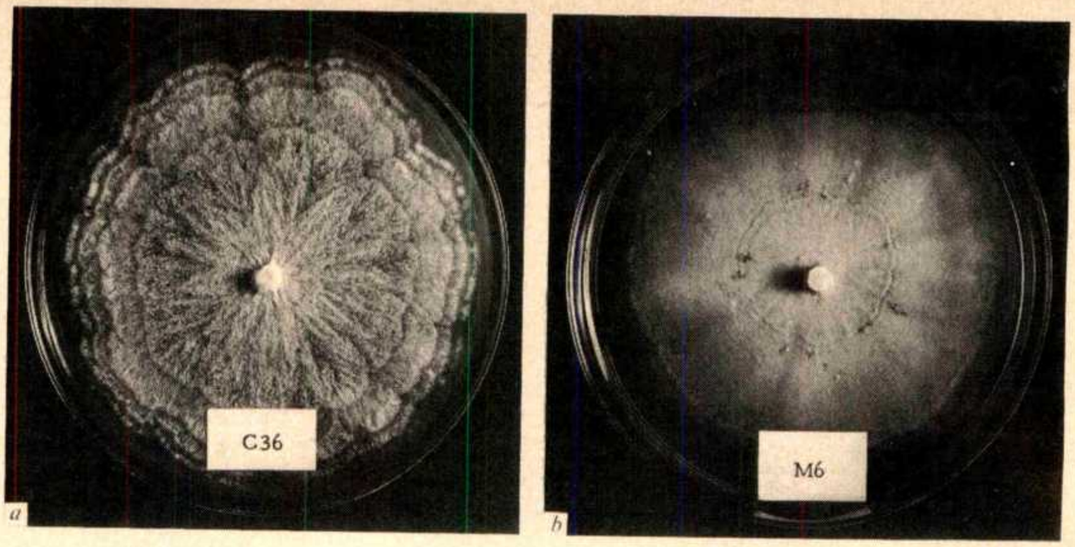

Fig. 1 Cultures of *C. ulmi* on 2% malt agar after 1 week in darkness at 18° C followed by exposure to light. *a*, Typical fluffy isolate from Chichester (Sussex); *b*, waxy isolate from Moreton (Oxfordshire).

disease situations. These included (*a*) the three main outbreak areas as identified in the 1971 survey; (*b*) recent outbreak areas, where a new centre of the disease was in evidence; and (*c*) non-outbreak areas where the disease was at its endemic level. Mass isolates were made from separate trees and single spore cultures derived; approximately 30 isolates were obtained from each locality.

Two Strains of *C. ulmi*

When radial growth rate experiments were run on 2% 'Oxoid Malt Agar' a relationship between growth rate and cultural morphology was established, and two groups of isolates could be distinguished. In one group the isolates were fast growing, with aerial mycelium aggregated into radial strands giving the culture a fibrous striate appearance. Clear zone lines were formed in response to diurnal fluctuation in light. These isolates were termed "fluffy" (Fig. 1*a*). Isolates of the second group were slow growing, the majority with a waxy yeast-like appearance, sparse aerial mycelium and little zonation (Fig. 1*b*). Fluffy isolates were remarkably uniform in cultural morphology, whereas the waxy isolates were more variable, both in degree of waxiness and in amount of aerial mycelium. There was virtually no overlap between the two groups on the basis of growth rate, and the great majority of isolates could be typed on this character alone.

Direct examination of the connexion between cultural characters and pathogenicity was made in comparative growth rate and inoculation experiments with 50 isolates from the samples. These were selected isolates from established outbreak, recent outbreak and non-outbreak areas together with the original five aggressive and five non-aggressive isolates[2]. Radial growth rates on 2% 'Oxoid Malt Agar' at 18° C were measured after five days in a replicated experiment. In pathogenicity tests, four-year-old clonal rooted cuttings of *Ulmus procera* (mean height 1.6 m) were inoculated in June 1972. The isolates were applied in randomized blocks with five replicates. Using the same inoculation technique as in 1971 (ref. 2), each tree received 5×10^5 spores. Disease was recorded in terms of percentage defoliation after two and four weeks, and as percentage stem dieback after eight and fourteen weeks.

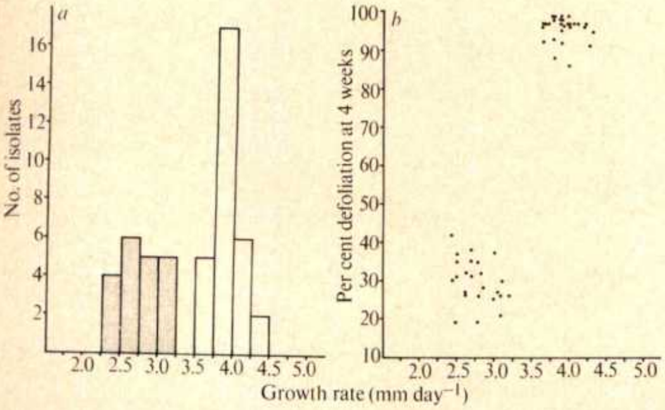

Fig. 2 *a*, Distribution of growth rates of fifty *C. ulmi* isolates showing the separation of fluffy and waxy groups. Tinted columns, waxy isolates; white columns, fluffy isolates. *b*, Relationship between growth rate and pathogenicity of the isolates.

The growth rate distribution of the isolates given in Fig. 2*a* shows the complete separation of the two groups. Fig. 2*b* shows the relationship between growth rate and pathogenicity; the complete separation of the two groups is again evident. The striking difference between the pathogenic behaviour of the groups is shown in Table 1. Defoliation proceeded rapidly with the fluffy type, under 5% of the leaves remaining after four weeks. By eight weeks, nearly 90% stem dieback had occurred, and after fourteen weeks only four of the 150 trees inoculated remained alive. In contrast, defoliation never exceeded 30% with the waxy type, dieback was slight, and inoculated trees frequently produced recovery shoots on the affected branches.

Table 1 Mean Growth Rate and Pathogenicity of Fluffy and Waxy Groups of *C. ulmi*

Item	Fluffy (n=30)	Waxy (n=20)
Growth rate mm day^{-1}	3.94 (±0.04)	2.50 (±0.16)
Pathogenicity		
% Defoliation		
At 2 weeks	46.7 (±1.37)	24.2 (±1.37)
At 4 weeks	95.9 (±0.57)	30.1 (±1.37)
% Stem dieback		
At 8 weeks	88.3 (±1.79)	12.9 (±0.90)
At 14 weeks	99.4 (±0.40)	13.7 (±0.91)

n, No. of isolates. $P < 0.001$ for all differences between means of fluffy and waxy groups.

The correlation between cultural characters and pathogenicity has enabled us to make a preliminary assessment of the relative frequency of the two strains, aggressive and non-aggressive, in different disease situations (Table 2). Of more than 350 cultures examined in 1972, only three have been found which could not be confidently assigned to one of the two groups.

Results showed that both strains were present in the outbreak situation with the aggressive strain predominant; in the non-

Table 2 Frequency of Aggressive and Non-aggressive Strains of *C. ulmi* in Different Disease Situations

Disease situation	No. of isolates Aggressive	Non-aggressive
(a) Main outbreak		
Chichester (Sussex)	30	9
Orsett (Essex)	35	1
Tewkesbury (Gloucestershire)	28	8
(b) Recent outbreak		
Frensham (Surrey)	30	6
Ilchester (Somerset)	17	5
(c) Non-outbreak		
Moreton (Oxfordshire)	0	36
Swindon (Wiltshire)*	0	5
Botley (Oxfordshire)*	0	4

* Sampling limited by availability of material.

outbreak areas only the non-aggressive strain was found. The Moreton situation is particularly interesting as it represents a "flare-up" of the strain. A number of trees died in 1970 but no further deaths have occurred.

C. ulmi in Europe and North America

Evidence for the non-aggressive nature of four isolates from the Netherlands has been presented[2]. Examination of these isolates has shown them to be of the waxy type, and a further eleven isolates, six from the Netherlands and five from northern France, were similar. It seems that, at least in parts of north-west Europe, the non-aggressive strain is the predominant if not the only strain to be found.

Of nine cultures from different parts of the United States, seven resembled the aggressive strain in growth rate and morphology, and two the non-aggressive. In an inoculation experiment, three of the former were compared with three aggressive and three non-aggressive British isolates on four-year-old trees of Commelin elm, of a clone of *Ulmus wallichiana* (301) and of seedling *U. americana*. Disease was recorded in terms of defoliation and stem dieback (Table 3).

The three American isolates were similar in pathogenicity to the British aggressive isolates in all elm varieties. The results of this limited comparison indicate that a strain of *C. ulmi* with similar characteristics to the British aggressive strain exists in the United States. The difference in pathogenicity between British aggressive and non-aggressive isolates was pronounced on Commelin and *U. wallichiana* but not on *U. americana*, which was highly susceptible to the non-aggressive isolates. This interaction demonstrates that Commelin and *U. wallichiana* have a form of resistance which is not possessed by *U. americana*, perhaps a major gene. On this supposition the aggressive strain would possess the virulence gene to overcome this resistance and the non-aggressive would not.

Table 3 Pathogenicity of North American and British Aggressive and Non-aggressive Strains of *C. ulmi*

Origin of isolates	Percentage defoliation after 4 weeks Commelin ($n=4$)	*U. wallichiana* ($n=3$)	*U. americana* ($n=2$)	Percentage stem dieback after 14 weeks Commelin ($n=4$)	*U. wallichiana* ($n=3$)	*U. americana* ($n=2$)
N. America						
(1) Athol (Mass.)	44	29	45	65	51	90
(2) Newhaven (Conn.)	24	32	65	28	48	90
(3) Kenilworth (Ill.)	50	40	57	72	63	92
Britain, aggressive						
(4) Essex	36	40	50	60	51	80
(5) Gloucestershire	36	33	63	74	47	96
(6) Sussex	55	45	52	59	68	93
Britain, non-aggressive						
(7) Cambridge	0	6	45	3	0	58
(8) Oxfordshire	0	2	67	0	0	82
(9) Denbighshire	0	4	37	0	0	54

n, No. of replicates.

Implications for the Dutch Elm Disease Problem

These results have considerable implications. First, recognition of the aggressive strains in culture has significance for the current disease situation in Britain, where an explosive epidemic is developing within a host population previously in equilibrium with the disease. It enables a ready distinction to be made between primary foci of the aggressive strain and local "flare-ups" of the non-aggressive strain, and it allows the aggressive strain to be detected in advance of the main disease front.

Second, the discovery of a correlation between cultural characteristics and pathogenicity is important for future research on the physiological basis of pathogenicity. Whether a faster growth rate can in itself account for the enhanced pathogenicity of the aggressive strain should be studied. Other morphological and physiological characteristics may well be found to be important.

The correlation also provides an opportunity for a study of genetic aspects of the disease. It is hoped that the survey of the compatibility types of British isolates now in progress will allow analysis of the genetic control of cultural variation and in particular the control and origin of aggressiveness. The relatively uniform appearance and behaviour of the aggressive isolates suggest that these are highly isogenic, possibly with a recent origin from a single clone. In contrast the waxy isolates may represent a sample of variation from the endemic gene pool.

Finally, some evidence has been presented that in the Netherlands and adjacent areas of north-west Europe a waxy non-aggressive strain appears to be predominant, whereas in the United States isolates of *C. ulmi* resembling the aggressive strain can be found. These observations are historically significant. Dutch elm disease was first described in Western Europe in 1918, and in Britain disease severity reached a peak between 1931 and 1937, and then declined. A high proportion of the elm population survived[3]. In Holland the disease was more destructive[4], but in recent years there has been little infection among remaining elms. The disease spread from Europe to the United States about 1930, resulting in continuous heavy losses, and it has progressed across the continent. A possible explanation is that an aggressive strain was originally prevalent in all three countries. Supporting evidence is provided by contemporary descriptions of cultures with "fluffy type" morphology in the United States[5], and in Europe[6,7]. After this time for some reason the aggressive strain declined within the *C. ulmi* population of Britain and Europe, but not in the United States. We may now be witnessing its reappearance in Britain.

Whatever the exact course of events, it would appear that isolates of *C. ulmi* available in Europe in recent years for screening elm material for resistance have not provided a sufficiently stringent test. This underlines the necessity of incorporating as much variation in pathogenicity of the fungus as possible in programmes of breeding for resistant elms.

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On the Origin of Deuterium

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The origin of deuterium has always been a problem for theories of stellar nucleosynthesis. A general solution is proposed and shown to be applicable under several astrophysical circumstances in the light of new observations of the Galactic abundance of deuterium.

Cesarsky, Moffet and Pasachoff[1] have recently observed an absorption feature in the spectrum of radiation from the Galactic centre at 327.38837 ± 0.00001 MHz. They interpret this as arising from the ground-state hyperfine transition in deuterium near 91.6 cm which is analogous to the well-known 21 cm line of ordinary hydrogen. If they assume the feature observed to be due to noise they are able to set an upper limit

$$\mathrm{D/H} < 5 \times 10^{-4}$$

while an analysis assuming the feature to be due to deuterium yields

$$3 \times 10^{-5} < \mathrm{D/H} < 5 \times 10^{-4} \qquad (1)$$

These results are to be compared with the terrestrial value of 1.5×10^{-4} and to the upper limit for the proto-solar value of 3×10^{-5} (refs. 2, 3).

Jefferts, Penzias and Wilson[4] report line emission from a cloud within the Orion Nebula at 144,828 MHz and attribute it to the $J=2$ to $J=1$ transition in DCN. In a separate investigation of the $J=1$ to $J=0$ transition at 72,414 MHz, the hyperfine components expected for DCN have also been found[5], setting the identification beyond reasonable doubt. The cloud in question probably has dimensions of the order of a light year and a mass of order $10^2\ M_\odot$, considerably less than the Orion Nebula itself. The H II region of Orion, which is the part seen optically, has mass $\sim 10^3\ M_\odot$, whereas a larger scale molecular cloud, detected in the 2.6 mm radiation of the CO molecule, has been estimated by Solomon (private communication) to have mass $\sim 10^5\ M_\odot$.

The emission from the $J=1$ to $J=0$ transition is approximately as strong as that in $^1\mathrm{H}^{12}\mathrm{C}^{15}\mathrm{N}$ and $^1\mathrm{H}^{13}\mathrm{C}^{14}\mathrm{N}$, so

$$\mathrm{D/H} = 6 \times 10^{-3} \qquad (2)$$

a remarkably high value. The ratio determined in this way applies to D and H in combination with CN, not to D and H in atomic form. Thus the D/H ratio in the interstellar gas could still be comparable with the terrestrial value, or with the value of 3×10^{-5} referred to above.

The position concerning deuterium has therefore changed from doubt concerning its widespread existence in the Galaxy to one in which it is a reasonable inference that D/H of order 10^{-4} occurs on a large scale, and the problem of the origin of deuterium now seems more urgent than it did before. Together with R. V. Wagoner[6], we found some years ago that significant quantities of D could arise in a low density Friedmann universe. Defining a parameter h from the relation (applicable after e$^{\pm}$-pair annihilation in the universe)

$$\rho_b = h T_9^3 \ \mathrm{g\ cm^{-3}} \qquad (3)$$

where ρ_b is the baryon mass density and T_9 is the radiation temperature measured in units of 10^9 K, we found D/H comparable with the terrestrial ratio of 1.5×10^{-4} when $h \simeq 6 \times 10^{-6}$. Setting $T_9 = 2.7 \times 10^{-9}$ K for the present temperature leads to $\rho_b \simeq 10^{-31}$ g ml.$^{-1}$ for the present baryon density, which is in good agreement with estimates which have been made of the average density of matter in galaxies by Oort[7] and Shapiro[8].

It is an unexpected feature of such a primordial mode of synthesis that the well-known cosmological parameter q_0 turns out to be small, and close to zero[6], instead of the value 0.5 required to "close" the universe. Many cosmological investigations, the formation of galaxies for example, are much more awkward in hyperbolic models ($q_0 \simeq 0$) than they are for $q_0 \geq 0.5$. One might seek to evade the resulting difficulties by arguing that, unlike an idealized Friedmann model, the actual universe is inhomogeneous. It might be supposed that the initial state of the universe was very patchy, with h falling below 10^{-5} in some places. On the other hand, the 2.7 K radiation background is exceedingly uniform, both locally and from one part of the sky to other distant parts of the sky. This uniformity, while not forbidding sufficiently fine scale inhomogeneities, would seem to us to constitute a warning against this line of argument.

It is also important in the new circumstances of the problem to reconsider possible astrophysical modes of origin for deuterium. Should it turn out that D/H is locally variable, astrophysical processes would be preferred to primordial synthesis, but if the D/H ratio is found to be universal then primordial synthesis would be preferred.

Investigations going back to the middle nineteen fifties have repeatedly shown that D is best produced astrophysically under non-thermodynamic conditions. We imagine α particles projected at high speed into an ionized gas composed mainly of hydrogen. If the gas temperature has some moderate value, say 10^5 K for definiteness, nuclear reactions leading to D production can occur. D can be knocked out of an α particle by a spallation reaction, and neutrons knocked out of the ^{4}He can subsequently be captured by protons of the ambient gas. For example, α particles entering gas at speed $c/3$ have a kinetic energy relative to the gas of ~ 200 MeV, which is 50 MeV per nucleon, and at such a bombarding energy the total cross section for all the reactions leading to D production is about 5×10^{-26} cm^2, that is, 50 mb according to Audouze *et al.*[9]. Although the stopping cross section due to Coulomb scattering is greater than this, it is clear that a significant fraction of the α particles will produce a D nucleus. Because the D is thus formed within a comparatively low temperature gas it is not subject to subsequent breakup, except in rare cases where it happens to be hit by a further incoming α particle.

There are many ways in which this general idea can be used; for example, it can be applied to cosmic rays entering a cloud of gas. The production of D (and ^{3}He) through the spallation of ^{4}He was discussed a decade ago[10] in connexion with magnetic flares in the solar surface. The nuclear physics involved is largely independent of the acceleration mechanism. But processes involving cosmic rays are not capable of explaining large D concentrations of the kind that have now been reported. Cosmic rays are too wasteful of their energy in this respect. D production reaches the geometrical cross section and thus occurs most efficiently when the energy per nucleon is about 30 MeV. Energies as high as several GeV, which is where the main reservoir of cosmic ray energy lies, are not required. For greatest efficiency we must look therefore to processes involving speeds $\sim c/3$.

Such speeds have indeed been found for shock waves generated by stellar explosions[11]. The shock wave starts in the region of the explosion at a speed not much different from the speed of sound, which is always much less than c. As it travels outwards into the lower density regions of the envelope, however, the wave speeds up. It is therefore in the outer envelope that speeds of the required order have been reported in previous investigations.

The shock wave condition we have in mind can be applied much more generally than to a supernova. The basic requirement is for a supply of radiant energy (or of relativistic particles) to emerge from some local source into a diffuse outer envelope of gas containing ^{4}He. The larger the energy supply the better. For a supernova we expect $\sim 10^{50}$ erg to be available, which is much less than a case reported recently by Appenzeller and Fricke[12–14]. Their work is concerned with objects having masses between 10^5 and 10^6 $M_\odot$—that is, masses of the order of the whole Orion Nebula. Under suitable conditions nuclear energy generation in a time scale of a few thousand seconds, yielding $\sim 10^{56}$ erg, can lead to expansion and disruption of the whole object. Because most of the energy is taken up in the radiation field, it is possible that a bubble of radiation, say with total energy $\sim 10^{55}$ erg, may work its way to the outer part of the object and may propagate thence into a surrounding diffuse cloud. Outbursts involving relativistic particles, also with energies of $\sim 10^{55}$–10^{56} erg, occur in radio galaxies. Indeed, outbursts from radio sources involving energies up to $\sim 10^{60}$ erg have been considered.

The energy in question, whether radiant or in the form of relativistic particles, would escape from the source at speed c if it were not for the material of the surrounding envelope. But as the envelope becomes more tenuous the radiation is able to push material ahead of it at speeds which approach more and more to c. In such circumstances the material of the envelope is accelerated forward impulsively at a shock front, and nuclei present in it are subject to spallation if the shock becomes violent enough. Deuterium is then formed, either by direct spallation of ^{4}He or from neutrons coming from ^{4}He, the neutrons being captured subsequently by protons downstream of the shock.

The properties of shock waves are usually investigated through the equations of continuum mechanics. The complex physical processes taking place at the shock front are idealized by a discontinuity, much as an impulse to a body is idealized in classical mechanics. We define v_i, v_s as velocity components normal to the shock, with subscripts i, s referring to conditions upstream and downstream of the front respectively. For simplicity, taking hydromagnetic effects to be small, and taking a frame of reference in which the front is stationary, we have the following conservation relations across the front:

$$\begin{gathered}\rho_i v_i = \rho_s v_s \\ p_i + \rho_i v_i^2 = p_s + \rho_s v_s^2 \\ u_i + \frac{p_i}{\rho_i} + \tfrac{1}{2} v_i^2 = u_s + \frac{p_s}{\rho_s} + \tfrac{1}{2} v_s^2\end{gathered} \tag{4}$$

where p is the pressure and u is the internal energy per unit mass. Terms in p_i, u_i are small in our case. Omitting them, we can satisfy equations (4) with

$$\rho_s = \rho_i \frac{\gamma+1}{\gamma-1}, \quad v_s = v_i \frac{\gamma-1}{\gamma+1}, \quad p_s = \frac{2\rho_i v_i^2}{\gamma+1} \tag{5}$$

where

$$(\gamma-1)\,\rho_s u_s = p_s \tag{6}$$

γ is the ratio of specific heats downstream of the shock, and is close to 4/3 in a radiation dominated problem. Putting $\gamma = 4/3$ in equation (5) we get

$$\rho_s = 7\rho_i, \quad v_s = v_i/7, \quad p_s \simeq \frac{1}{3} a T_s^4 = \frac{6}{7} \rho_i v_i^2 \tag{7}$$

The third of these equations can be regarded as determining v_i when T_s and ρ_i are given. The value to be used for T_s depends on the energy supply, while ρ_i is the density of the envelope upstream of the shock. From here on, we shall be concerned with situations in which T_s is high enough in relation to ρ_i for the resulting value of v_i to be of order $c/3$.

Material flowing through the front experiences a change of velocity $v_i - v_s = 6v_i/7$, which for $v_i = c/3$ is $2c/7$. If we now think of the material in terms of individual particles, instead of from the point of view of continuum mechanics, the particles experience a change in velocity of $2c/7$ as they pass from being upstream to being downstream of the shock. We have to think of the front as possessing a finite depth and of particles from upstream experiencing collisions as they pass through a finite shock zone. As a velocity of $2c/7$ is equivalent to a bombarding energy of ~ 40 MeV per nucleon we have a situation similar to that discussed above for α particles projected into a stationary gas. Thus ^{4}He present in material upstream of the shock will be subject to fragmentation as it passes through the front.

The present situation is actually more favourable to fragmentation than the case of α particles projected into an ambient gas, because all particles in the shock zone have come from upstream and have therefore experienced collisions. About half of the bombarding energy will be transferred to electrons, but otherwise the bombarding energy will be retained as random motions of protons and α particles within the shock zone, and the α particles will therefore be subject to breakup over the whole of the time they are within the shock zone.

Material may be considered to have flowed downstream of the shock when electrons have had sufficient time to radiate the kinetic energy they have acquired from the heavy particles. Radiation through bremsstrahlung occurs with cross section

$$\sigma_{\text{brems}} \simeq 4 \frac{e^2}{\hbar c} \left(\frac{e^2}{mc^2}\right)^2 \ln(2E) \tag{8}$$

where E is the electron energy in units of the rest mass. In our case the electron energies are ~ 20 MeV, and the logarithmic term in equation (8) is about 4, so the cross section is ~ 10 mb. This is about five times less than the spallation cross section. On the other hand, an electron of energy 20 MeV has a velocity about five times greater than a proton of the same energy. Hence

$$\langle \sigma v \rangle_{\text{Bremsstrahlung}} \simeq \langle \sigma v \rangle_{\text{Spallation}} \tag{9}$$

from which it follows that an appreciable fraction of the α particles must be fragmented by the time they pass downstream of the shock.

At this stage we have to distinguish two cases according to whether the gas density is high enough for neutrons from spallation to be captured by protons, or not. The former case is more efficient in its deuterium production by an order of magnitude. Considering this case, and taking the material of the initial cloud to have the usual helium concentration of ~ 0.25 by mass, and using say 40% for the fraction of the helium experiencing complete spallation, we arrive at a D concentration downstream of the shock of 0.1. Thus the mass density of D downstream of the shock is 0.1 ρ_s. Using (7), and setting $\nu_i = c/3$, we have

$$\rho(D) = 0.1\ \rho_s = \frac{7}{10}\ \rho_i = \frac{7}{10} \times \frac{7}{18}\ \frac{aT_s^4}{\nu_i^2}$$

$$= \frac{49}{20}\ \frac{aT_s^4}{c^2} = 2.7 \times 10^{-21}\ aT_s^4 \qquad (10)$$

or $$aT_s^4/\rho(D) = 3.7 \times 10^{20}\ \text{erg g}^{-1}$$

This is a relation between energy supply and deuterium production. The energy "cost" in the radiation field to produce one gram of deuterium is seen to be $\sim 3.7 \times 10^{20}$ erg. So to produce an average D/H ratio equal to the proto-solar value of $\sim 3 \times 10^{-5}$ throughout a mass M requires $\sim 10^{16}\ M$ erg, from which we see that to obtain D/H $\sim 3 \times 10^{-5}$ throughout the Galaxy requires $\sim 3 \times 10^{60}$ erg. Because this value is within the range that can be contemplated it seems possible for the present process to give a galactic deuterium concentration comparable to the initial solar system value.

The present considerations require neutrons from the spallation of ^{4}He to be captured by protons. For this condition to be satisfied ρ_i must not be much less than $\sim 10^{-8}$ g cm^{-3}. Otherwise the efficiency of D production is reduced by an order of magnitude, and the energy requirement is increased correspondingly. In the rest of this article we shall take $\rho_i = 10^{-7}$ g cm^{-3} for definiteness, and will consider the rates which are then operative for various processes.

The first question to be asked is: what will be the order of the depth of the shock zone? Taking $\sim 3 \times 10^{-7}$ g cm^{-3} as the average density within the shock zone, and noting that $\langle \sigma \nu \rangle_{\text{Bremsstrahlung}} \simeq 3 \times 10^{-16}$, we see that the electrons lose their energy in a time $\sim 2 \times 10^{-2}$ s. In this time material flowing at a mean speed of say $\sim \nu_i/2 = c/6$ travels a distance $\sim 10^8$ cm. This gives the order of the depth of the zone.

To prevent radiation downstream of the shock from simply streaming through the front it is necessary that the optical depth of material within the shock zone shall be greater than unity. For the numerical values considered in the previous paragraph there are about 30 g of material per unit area of the front. This is sufficient to dam back the radiation through Thomson scattering by the electrons. Before the radiation can penetrate the shock zone new material is then added from upstream. This circumstance does not depend on the particular numerical values used here. It depends essentially on the Thomson scattering for radiation being much larger than the bremsstrahlung cross section, $\sim 10^{-24}$ cm^2 compared with $\sim 10^{-26}$ cm^2.

Once bremsstrahlung transfers energy from the electrons to the radiation field other processes become involved, particularly Compton scattering. Because most of the bremsstrahlung energy from 20 MeV electrons consists of γ rays above 1 MeV, Compton scattering has a complex behaviour, certain scattering angles augmenting the radiation field, others transferring energy back to the electrons. A refined calculation would be necessary in order to consider such effects in detail. Here we shall simply take relation (9) to represent the order of magnitude of the relation of radiation losses to spallation. The conclusion from (9) is that an appreciable fraction of α particles are fragmented by the time they pass downstream of the shock.

Deuterium produced within the shock zone will itself be subject to spallation, as will be ^{3}He and T. Consequently we shall not regard D production as being due to the immediate spallation of ^{4}He, but as arising from neutrons released in the breakup of ^{4}He. The lifetime of the neutrons against weak decay ($\sim 10^3$ s) is very long compared to the time spent ($\sim 10^{-2}$ s) in the shock zone. So the neutrons move downstream to regions where thermodynamic conditions can be considered to be established. Putting $\rho_i = 10^{-7}$ g cm^{-3}, $\nu_i = c/3$ in (7) gives $T_s \simeq 7.6 \times 10^6$ K, which is far too low for deuterium formed by $n + p \rightarrow D + \gamma$ to be subject to spallation or to photodisintegration. The $\langle \sigma \nu \rangle$ value for this reaction is 7×10^{-20} cm^3 s^{-1}, so for a hydrogen density $\simeq 7 \times 10^{-7}$ g cm^{-3} downstream of the shock it takes some 30 s for the neutrons to be captured by protons. Because this is much less than the neutron half-life, although amply long enough for the neutrons to flow downstream well clear of the shock, we conclude that essentially all neutrons go to form D.

To recapitulate to this point: Normal thermonuclear processes generate ^{4}He from hydrogen with very little production of deuterium. But if ^{4}He can be shaken loose into its constituent neutrons and protons in abnormal situations, such as those in the front of a high speed shock wave, conditions become favourable to D production provided the gas density is not so small that the neutrons decay before they are captured by protons. Conditions are then also favourable in that the temperature $T \simeq 7.6 \times 10^6$ K behind the front leads to a lifetime for D(p,γ)^{3}He of $\sim 10^{10}$ s, which is much longer than the time required for a local exploding object to disperse. The D/H ratio can be locally higher than the terrestrial value by as much as 10^2, but after averaging with other exterior material the D/H value will be lowered. If the estimate of 3×10^{-5} for the proto-solar value is typical of the interstellar medium as a whole, then the process described here could be the origin of all the deuterium in the Galaxy. Accompanying the production of D in the shock front will be that of a smaller amount of ^{3}He, perhaps enough to yield the proto-solar values ($\sim 10^{-5}$) taken by Black[3] as typical. Further, because the explosion which produces the shock wave may well be due to nuclear energy generation converting a substantial fraction of hydrogen into helium, this process may also be the source of galactic ^{4}He. This brings us back (see pp. 23, 24 of ref. 6) full circle to the fact that conversion of hydrogen into helium in one part in four by mass yields the full energy of the background microwave radiation at 2.7 K and once again forces us to ask if there could have been a mechanism which provided the necessary thermalization. So far we have found no plausible affirmative answer to this question, but the coincidence of the numbers remains puzzling.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Fine Structure of the Jupiter Radio Bursts

SHORT pulses with a time scale of milliseconds and fractions of a millisecond have been observed in the radio emissions of Jupiter at wave frequencies near 20 MHz since 1956 (refs. 1 and 2). Little is known about these "S" bursts, however, although it has been established[3] that their occurrence depends strongly on the orbital position of the satellite Io. Further, Gordon and Warwick[4] were able to show from a small set of observations that the bursts may have a relatively narrow radio frequency bandwith (<50 kHz) and that their centre frequency may change rapidly with time at the rate 25–35 MHz s^{-1}, at least near 26 MHz.

Ellis[5] predicted that radio bursts with these general frequency-time characteristics may result from the passage of electron streams of about 10 keV energy through the spatially varying magnetosphere of Jupiter, although further work along these lines was handicapped by the inadequate detail of the available spectrograms. These had a time resolution of 10 ms and a frequency resolution of 50 kHz. An improvement in each of these parameters of at least an order of magnitude seemed to be essential to reveal the fine structure of the bursts.

In the observations reported here a time resolution of 0.5 ms combined with a frequency resolution of 10 kHz has been attained at radio frequencies using the technique of time-expansion spectrographic analysis previously used in the audio frequency range (ref. 6 and a private communication from R. L. Dowden). Signals received in the frequency range 15–18 MHz were reduced in frequency to 0–3 MHz and recorded on a standard helical scan video recorder. The video tape was subsequently replayed in the single frame replay mode at the rate of one 20 ms frame every 8 s. A single channel sweep frequency spectrograph with a bandwidth of 10 kHz, a frequency range 0–3 MHz and a sweep time of 8 s analysed the frequency-time information in each frame. No internal modifications to the video recorder were necesssary. The antenna which was used was a new general purpose radio telescope in the form of a filled aperture array, 2,000 foot square (ref. 7). It has a continuous frequency range of 2–20 MHz and operates as a transit instrument with four independent beams under computer control. The positioning of the beams takes 2 ms.

One beam was switched to the declination of Jupiter for ten minutes each day between May and September 1972. Video recordings were made of the signals, mostly between 15 and 20 MHz, while chart records were made of the signal intensity at six frequencies between 2 and 20 MHz. Several real time sweep-frequency spectrum analysers were used for low time resolution observations.

Video tape recordings of the rather rare S burst events were obtained during the transits of June 18 and September 13, 1972, some thousands of individual bursts being recorded. Figs. 1 and 2 show examples of different types of bursts observed on June 18. Most numerous were multiple quasi-periodic bursts with a frequency-time slope of 12.5 MHz and a frequency range of approximately 1 MHz (Fig. 1*a* and *b*) occurring at the rate of about 30 s^{-1}. Their bandwidth was in the range 10–50 kHz and single frequency duration 1–5 ms. The overall duration of each burst was about 60 ms. They probably correspond to the millisecond S bursts observed at fixed frequencies by Slee and Gent[2] and will be called S_1 bursts. Fig. 1*b* shows an example of a variant of the type S_1 in which a Z-shaped pattern was observed on the spectrograms.

A second class of burst is illustrated in Fig. 2*a*. These occurred at about ten times the rate of the S_1 bursts in a given time interval and showed both positive and negative frequency-

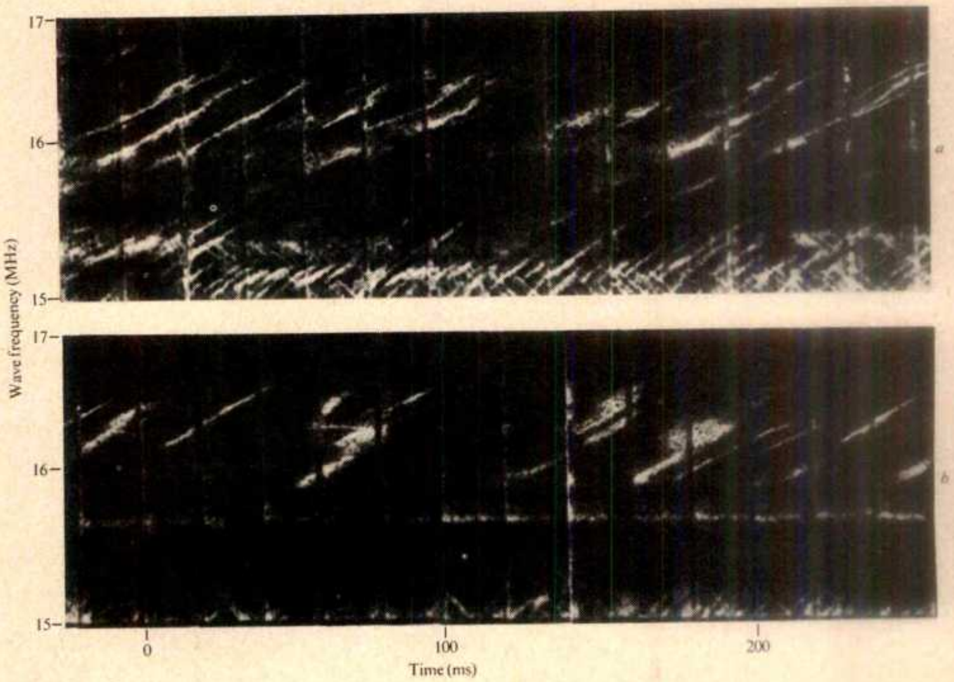

Fig. 1 *a*, Spectrograms of type S_1 Jupiter bursts recorded on June 18, 1972. Note the splitting of the frequency-time trace which can be seen in the extreme right-hand burst. The curvature of the traces towards the lower edge of each record is due to nonlinearity in the frequency sweep. *b*, Examples of a rare variant of the type S_1 burst in which the frequency-time trace shows a characteristic Z shape.

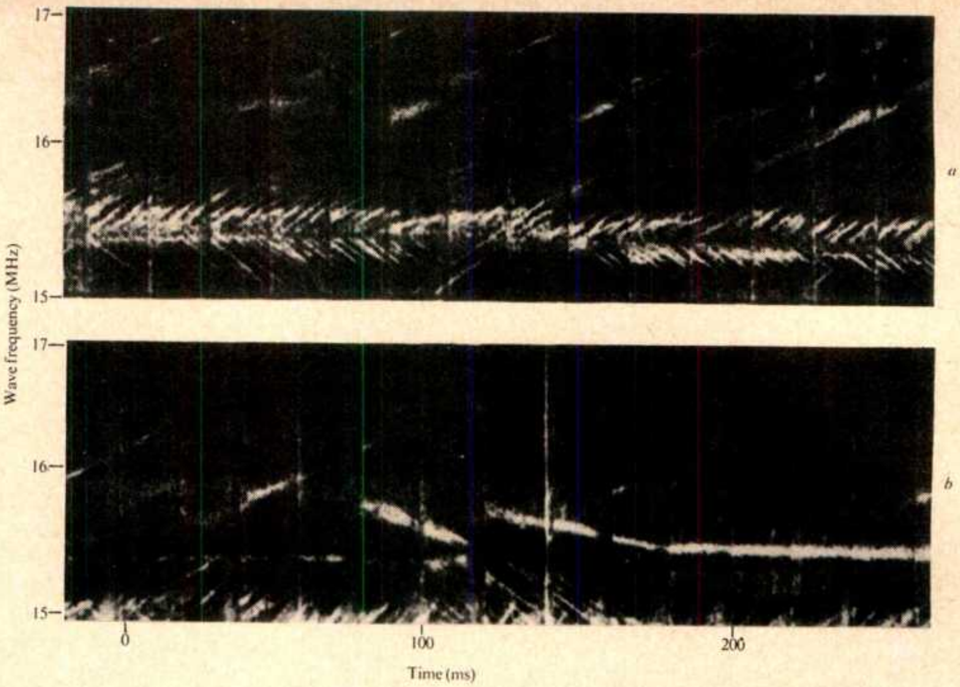

Fig. 2 *a*, Type S_2 herringbone bursts concurrent with type S_1; *b*, shows an example of a class of bursts of wider bandwidth and longer duration, typically 100 kHz and 0.1–1 s respectively.

time drifts of ~ 10 MHz s^{-1}, sometimes simultaneously. These S_2 bursts were somewhat similar to the herringbone solar radio bursts, and with a single frequency duration of a millisecond or less may correspond to the sub-millisecond bursts previously observed[2].

On a time scale of 100 ms, a class of bursts with no particular frequency-time slope (Fig. 2*b*) was recorded, their bandwidth being typically 100 kHz and overall duration 0.1 to 1.0 s.

The S_1 and S_2 bursts are shown in more detail in Fig. 3*a* and *b*, in which the signal amplitude is displayed as a function of frequency and time for a time duration of 20 ms and a frequency range of 200 kHz. The crossing of the frequency-time traces which can be seen near the lower edge of Fig. 1*a* is shown clearly in Fig. 2*b*.

The observed frequency-time slope of the bursts of 10–12 MHz s^{-1} at a wave frequency of 15 to 16 MHz is consistent

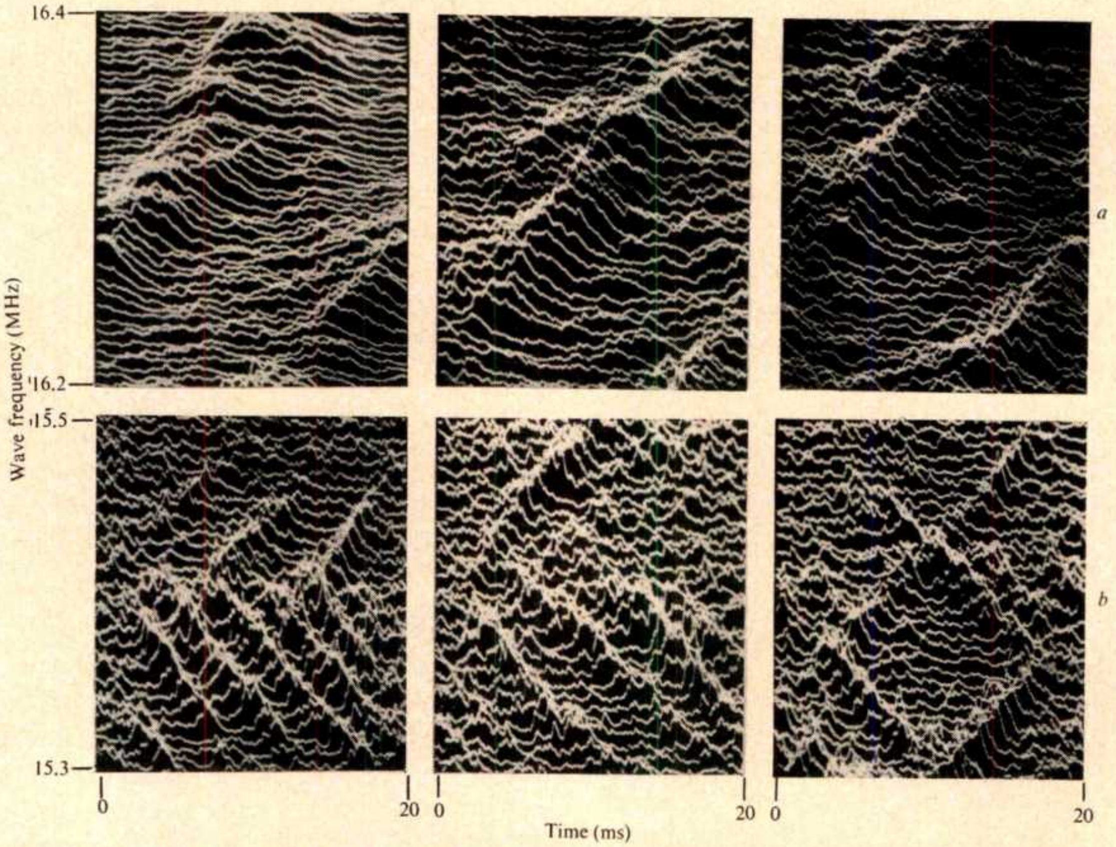

Fig. 3 Records showing examples of the variation of amplitude versus frequency and time of type S_1 (*a*) and type S_2 (*b*) bursts on an expanded frequency-time scale. The last section of *b* shows in more detail the crossing of the frequency-time traces which can be seen near the low frequency edge of Fig. 1*a*. Post-detection integration time constant 2.0 ms (*a*) and 0.5 ms (*b*). Frequency resolution of analyser 10 kHz. The separation of the traces in frequency is 5 kHz.

with the observations of Gordon and Warwick[4] of 25–35 MHz s^{-1} near 26 MHz if it is assumed that electrons of energy 8–10 keV were responsible on both occasions. The change in the frequency-time slope between the two frequencies is just that which would be expected if the radiated wave frequency is near the local cyclotron frequency of electrons in the magnetosphere[5] and if the rate of change of frequency with time arises from the longitudinal speed of the electrons and the spatial variation of the magnetic field.

As well as looking like solar radio bursts on the frequency-time plane, the herringbone bursts also bear a remarkable frequency-time resemblance to VLF emissions from the Earth's magnetosphere triggered by artificial electromagnetic wave transmissions from VLF ground stations[8]. It is believed in this latter situation that the incident electromagnetic radiation leads to coherent cyclotron radiation from a pre-existing electron stream in the vicinity of a region where the incident wave frequency, magnetic field intensity and electron energy are sufficient to satisfy the doppler-shifted cyclotron resonance condition[8]. The herringbone pattern would then arise from radiating electrons moving in both directions along a magnetic field line away from the resonance region.

It has been suggested[5,9] that the orbital motion of Io relative to the Jupiter magnetosphere causes the generation of Čerenkov electromagnetic radiation at low radio frequencies (of the order of 10^5 Hz) where the phase speed of propagation is less than the relative orbital velocity of the satellite. Calculation has shown that such radiation would travel inwards towards the planet along ray paths which would bring it into the regions above the Jupiter ionosphere, thought to be the source of the Io-controlled decametric radiation. In this event cyclotron resonance between the inward travelling radiation, electron streams of keV energy, and the outward decametric radiation might be expected to lead to the observed frequency-time patterns of the bursts.

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Further Data on the Corsica–Sardinia Rotation

The suggestion that the Corsica–Sardinia microplate rotated counter-clockwise with respect to France and Italy seems to be widely accepted today[1,2], but the dating of the rotation is still not satisfactorily settled. Alvarez[3], reviewing all data on hand, proposed an age of 11.5 m.y. for the start of the motion, and 6 m.y. as the time when the motion ended.

We now propose a different approach to this problem, based on the radiometric age of metamorphism in the Apuane Alps (Northern Tuscany, Italy)[4] and on the general tectonic picture of the Northern Apennines.

The Apuane Alps are located along the western (Tyrrhenian) coast of North–Central Italy, between the parallels of Pisa and La Spezia (Figs 1 and 2). Carrara is well known for its white marbles. From a geological point of view this mountain range, approximately 35 km long, is a tectonic window cut in the pile of nappes by which the northern Apennine is built up[5].

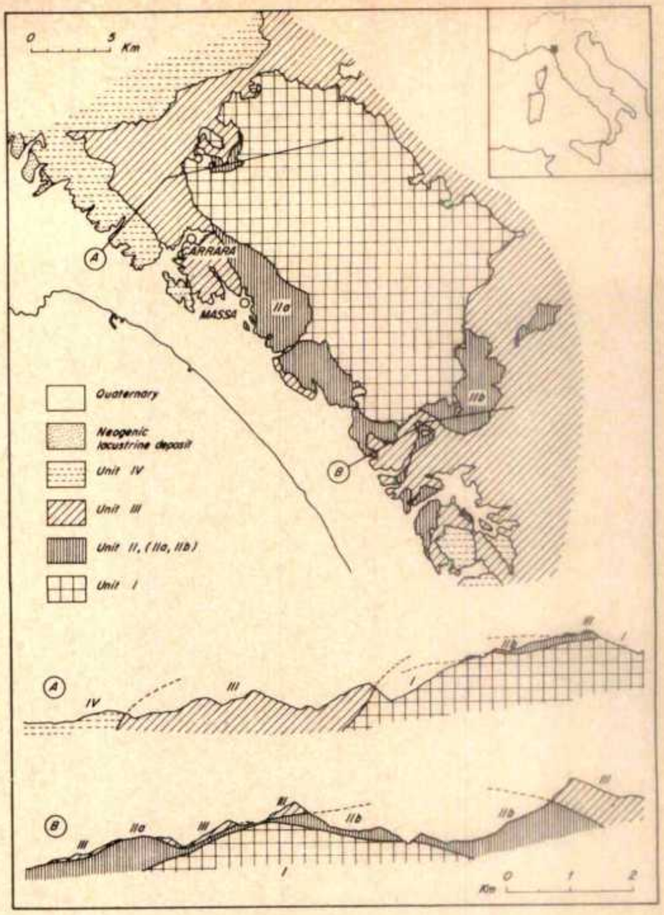

Fig. 1 Tectonic sketch-map and cross sections of the Apuane Alps. For comments see text.

Four tectonic units or groups of units are superimposed in the Apuane Alps. The lowest (Unit I), outcropping in the core of the massif, has at the base a phyllitic formation of undefined Palaeozoic age, then Permo-Triassic volcanics (of acidic type) and arkoses, Upper Triassic dolostones, Jurassic massive limestones, cherty limestones and radiolarites, then Cretaceous-Eocene marly shales, followed by turbiditic sandstones (possibly Oligo-Miocene).

Unit I is tectonically overlain by Unit II. The stratigraphy of Unit II is similar to that of Unit I, apart from small differences. The Triassic pre-carbonatic sequence is here represented by a thick group of detrital formations ("Verrucano") with calcareous lenses; Permian volcanics and their (partly) Triassic alteration products are lacking; also, evaporites are found associated with dolostones in the Upper Triassic deposits.

In Fig. 1, Unit II has been subdivided in two subunits (II*a* and II*b*) because its detrital base (subunit II*a*) chiefly outcrops in the western side of the Apuane Alps, with a peculiar tectonic style, and its Mesozoic carbonatic rocks and Tertiary flysches are found only in the southern and southeastern parts of the massif (subunit II*b*). Differences in metamorphism also justify this subdivision.

Unit III, the "Tuscan Nappe", is made up of a stratigraphical series ranging in age from Upper Triassic to Oligo-Miocene, in many aspects similar to the underlying units.

In turn Units I, II and III are covered by a complex pile of tectonic units, comprehensively called "Ligurids", which contain, among other rocks (such as the chaotic mélange known as "*argille scagliose*"), serpentines, gabbros and basalts.

Units I, II and III can be referred, broadly speaking, to a

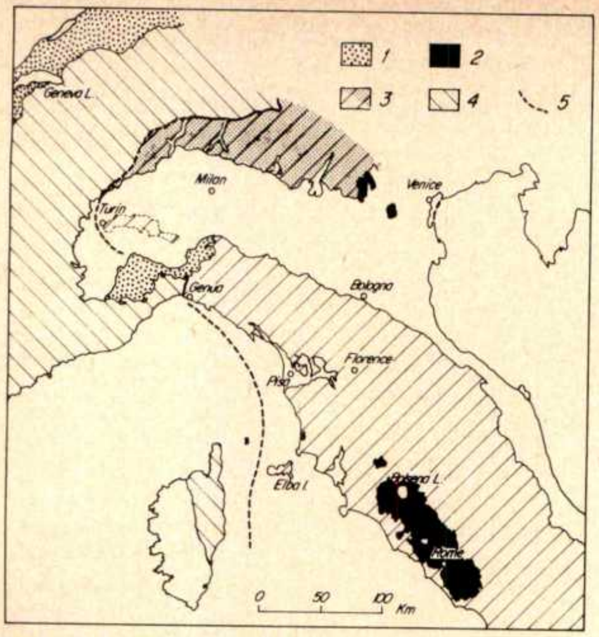

Fig. 2 Relations between Alps and Apennines north of the latitude of Rome. 1, Molassic peripheral basins. 2, Recent (tertiary and quaternary) volcanics. 3, Apenninic (not shaded) and Austro-Alpine Units (shaded). The outcrops of Apenninic rocks east of Turin (Monferrato hills) are partially covered by molassic deposits. 4, Alpine Units. Slabs of Apenninic Units involved in the tectonics of the Alps are not shown. 5, Separation line between Alps and Apennines.

continental shelf sedimentary basin, but the Ligurid complex indicates an oceanic environment.

Metamorphism affected the two lower units (I and II), contemporary with internal deformation; in Unit I it reaches the lower greenschist facies (paragenesis with quartz-albite-muscovite-chlorite). But subunit II*b* shows the same metamorphic grade as Unit I, and subunit II*a* underwent a stronger and different metamorphism (paragenesis with quartz-albite-muscovite-chlorite-biotite; presence of kyanite in some levels). These differences in metamorphism between II*a* and II*b* further justify the splitting of Unit II into two subunits. Unit III is not metamorphic.

The northern Apennine Range, of which the Apuane Alps are a part, is strictly connected to the Alps: these two ranges are undoubtedly paired from the latitude of the Corsica–Tuscany couple up to the Monferrato hills (which belong to the Apennines) between Genoa and Turin[6] (Fig. 2). The western Alps–northern Apennines system is flexed into a horseshoe shape, thus representing an orocline in Carey's sense[7].

The counter-clockwise rotation of the Corsica–Sardinia microplate is considered to be responsible for, or at least related to, the flexing in plan of the sedimentary basins out of which the northern Apennines originated.

In a pre-rotation reconstruction, Corsica and Sardinia were aligned in a NE–SW direction. The same was true for the sedimentary basins of northern Apennines and western Alps, which were limited to the NW by the European plate and to the SE by the Apenninic–Dinaric foreland. The middle of the trough, of oceanic (eugeosynclinal) nature, was occupied by the Ligurian and Piedmontese Units.

To the NW were the miogeosynclinal basins of western Alps (Briançonnais and Delphino–Elvetic), and to the SE those of the northern Apennines, in which Units I, II and III were forming. Most of the eugeosynclinal Ligurian Units were deformed during Eocene when they were thrust northwestwards on to the European block. Meanwhile sedimentation was still going on in the miogeosynclinal basins of the Apennines, where Units I, II and III were depositing.

At the beginning of the Miocene, after very thick turbiditic beds were deposited in these basins, compressional movements began to affect Units I, II and III. Metamorphism interested Units I and II together with internal deformation which was therefore characterized by a high degree of plasticity. At roughly the same time, units of the Ligurian complex, already partly folded and thrust over the European block, moved back towards the Apenninic foreland to the SE, where they were superimposed on Units I and II, together with Unit III (Tuscan Nappe). In this way they provided the load necessary for the accomplishment of metamorphism in Units I and II.

As the deformation wave in the Apennines progressed east or southeast, the various Units were deformed and successively thrust over the adjacent basins to the SE.

The occurrence of internal deformation and metamorphism prior to overthrusting can account for the independence of metamorphism of the place occupied by the Units in the tectonic succession; this is also confirmed for the different ages found for metamorphism of Unit I and subunit II*a*.

On the other hand deformation and metamorphism of the northern Apennines are only the latest events of a compressional history (most probably linked to the Corsica–Sardinia rotation), which must have begun some time earlier. Unless during the rotation the Corsica–Sardinia microcontinent moved as one block together with the Italian landmass (which was part of another plate) the rotation as described above must also have been connected to the consumption of the oceanic crust that was situated between Corsica–Sardinia and the Italian plate[8]. It is difficult to escape the conclusion that the folding of the northern Apennines is connected to the rotation of the Corsica microplate. Thus, metamorphism in the northern Apennines offers the opportunity for dating a late moment of the Corsica–Sardinia rotation.

Table 1 Dating of Metamorphic Muscovite Samples

Sample*		K%	ml. ^{40}Ar 10^{-5}/gK	rad. ^{40}Ar/ total ^{40}Ar	Age m.y.	
Unit I	A1	5.77	4.43	0.44	11.0	
	A2	6.18	4.49	0.79	11.2	average 11.3
	C1	7.85	4.70	0.64	11.8	
Subunit II*a*	B1	3.96	6.07	0.60	15.2	
	B2	2.62	6.12	0.51	15.3	
	B3	5.45	6.81	0.74	17.0	
	B4	2.52	5.86	0.35	14.5	average 14.6
	B5	3.32	4.83	0.41	12.1	
	B6	8.02	5.26	0.53	13.0	
	B7	4.70	6.25	0.43	15.3	
Subunit II*b*	P1	6.03	4.15	0.53	10.8	average 10.8
	P2	2.97	4.37	0.44	10.9	

* Sample numbers differ from ref. 4.

We dated the metamorphic muscovite which is found at many levels in Units I and II, especially in impure marbles and phyllites: after dissolving the calcareous fraction in acetic acid the mica was separated from other minerals of the residue, quartz, pyrite, chlorite, sometimes kyanite and epidote. The muscovite was analysed for K and Ar in a routine way. The results are shown in Table 1; further details are given in ref. 4.

Metamorphism in subunit II*a* ended at about 14 m.y.; in I and II*b* it lasted until 11 m.y.; this is a confirmation of the tectonic conclusions (thrusting of the allochtonous Units after a phase of internal deformation) that could be reached from the fact that II*a*'s metamorphism is higher than I's.

Because the metamorphism was contemporary with internal deformation, the age of 14 m.y. in subunit II*a* represents an upper limit for the beginning of compressional tectonic movements in the zone of northern Apennines and therefore for the start of the rotation of our microplate. The K/Ar method dates the end of the metamorphic reactions, so we must add to the 14 m.y. the time necessary for the metamorphism to take place.

The duration of single metamorphic episodes has been shown to have been between 2 and 10 m.y. in the Alps[9]. Even attributing to the metamorphism of subunit II*a* the minimum duration

(2 m.y.), we must push back the beginning of the metamorphism to at least 16 m.y.

Further, it is doubtful that metamorphism can be considered the first tectonic event in the evolution of the northern Apennines; that is, it must have been preceded by other tectonic events. This is particularly significant in the case of subunit II*a*, where metamorphism took place under a rather high *P*/*T* ratio, as shown by the presence of kyanite: the high pressure is to be attributed to a tectonic overcharge. Thus to the previously estimated limit of 16 m.y. more time must be added during which a series of compressional events preparatory to metamorphism took place. The age of 16 m.y. for the beginning of the rotation thus represents a lower limit; the upper limit remains undefined.

Regarding the rotation, the following considerations are of interest: with the Messinian (Pontian), distensive movements are recorded in the zone between Corsica–Sardinia and Tuscany. These movements, still active in some places, dissected the Tyrrhenian side of this mountain range in a series of horsts and grabens, and in a general way tended to increase the space between Corsica–Sardinia and Tuscany, thus acting in a sense contrary to the rotation. The rotation and the compression with it must have ended with the Messinian. As the Miocene–Pliocene limit in Tuscany is fixed at about 7 m.y., the end of the rotation must be set at least at 9–10 m.y.

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The Silica Budget of the Antarctic Circumpolar Current

THERE is disagreement as to whether the Antarctic Circumpolar Current is a major source of dissolved silica arising from the dissolution of glacier flour[1–3] or a sink due to sedimentation of diatomaceous opal[4,5].

The distribution of silica in the World Ocean is greatly influenced by biological factors. It forms the tests of radiolaria and diatoms which grow mainly in the surface waters. The resulting particulate phases, tissue, protoplasm and tests sink across the thermocline mixing-barrier into the deep waters: a variety of biological and inorganic mechanisms act to oxidize and redissolve a large fraction of this material both while it is sinking through the water column and while it is resting on the bottom. The net chemical effect of this process is to separate the biologically active and inactive dissolved components. The distribution of the latter is largely controlled by the mechanisms of primary injection, continental runoff, submarine weathering, precipitation and absorption, and the physical hydrodynamic processes of mixing and transport. Biological activity, however, acts to "strip" the required dissolved constituents from the surface layer and inject them into the deep layer. The return of both active and inactive components to the upper waters is by the same physical mechanisms.

The North Atlantic Deep Water (NADW) is formed from such "stripped" surface water which has been advected north from low latitudes[6]. Hence the concentrations of biologically active materials are extremely low in this water mass. On its southward flow the NADW encounters the eastward flowing Circumpolar Current at about 40° S after the latter's emergence from the Drake Passage. Geostrophic calculations[7] indicate that the Deep Water flow across 30° S latitude in the Atlantic is approximately 18 Sverdrup ($\mathrm{m}^3 \times 10^6\ \mathrm{s}^{-1}$). Reid and Nowlin[8] have recently determined the flux through the Drake Passage at 240 Sverdrup. The NADW is therefore almost completely assimilated in this massive current, its presence being indicated only by the broad salinity maximum in the Circumpolar Deep Water[9].

The Circumpolar Current itself is driven by the prevailing Westerlies whose core is centred at 45 to 50° S (ref. 10). Close to the continent the prevailing winds are easterly and at the divergence large-scale upwelling of Circumpolar Deep Water occurs[11]. A large fraction of this water flows east and north under the Westerlies until it encounters the warm, more saline sub-Antarctic surface water in a strong, stable, frontal region, the Antarctic Polar Front, characterized by a drop in surface temperature of several degrees in a few kilometres[11,12]. It is immediately north of the Front in a region of intense mixing that the Antarctic Intermediate water is formed.

The Southern Ocean receives much more water from precipitation than it loses by evaporation, the excess being about 50 cm yr^{-1} (ref. 13). The input of ice and melt-water from Antarctica is between 5 and 10 cm yr^{-1} (refs. 14, 15). Because these waters have extreme properties relative to the upwelling Deep Water, it is possible to estimate the flux of this latter component from salinity balance calculations[16].

An independent approach can be made using oxygen isotope data[17]. Evaporation and freezing result in quite small fractionation effects in oceanic surface waters while the progressive stripping of rain-water from weather systems leads to an increasing enrichment of the lighter isotope in the residual vapour. The general motion of weather systems is polewards from the areas of high evaporation in low latitudes so that the rain-water in the Circumpolar region has an $^{18}\mathrm{O}/^{16}\mathrm{O}$ ratio very different from the surface sea water. Defining $\delta^{18}\mathrm{O} = (R_{\mathrm{sample}}/R_{\mathrm{standard}} - 1) \times 1{,}000$ where the δ values are in per thousand, $R = {}^{18}\mathrm{O}/^{16}\mathrm{O}$ and the standard is Standard Mean Ocean Water, SMOW (ref. 18), the values for surface waters cluster around zero, for marine water vapour −10 to −14‰ (about 3‰ lighter than the equilibrium value[17]), and for high latitude precipitation −20 to −30‰. Craig and Gordon[17] estimated the average $\delta^{18}\mathrm{O}$ values for the various components of the water flux in the Antarctic Ocean (Table 1).

Assuming a balance between the flux of water and of oxygen isotopes into the mixed layer from the upwelling of Circumpolar Deep Water (V_{DS}) precipitation (V_{AS}) and continental ice and melt waters (V_{CS}) and the flux out as Intermediate Water (V_{SI}), Bottom Water (V_{SB}) and evaporation (V_{SA}) then

$$V_{\mathrm{DS}} - V_{\mathrm{SI}} - V_{\mathrm{SB}} + V_{\mathrm{AS}} - V_{\mathrm{SA}} + V_{\mathrm{CS}} = 0 \qquad (1)$$

$$V_{\mathrm{DS}}\,\delta_{\mathrm{D}} - V_{\mathrm{SI}}\,\delta_{\mathrm{S}} - V_{\mathrm{SB}}\,\delta_{\mathrm{SB}} + V_{\mathrm{AS}}\,\delta_{\mathrm{AS}} - V_{\mathrm{SA}}\,\delta_{\mathrm{SA}} + V_{\mathrm{CS}}\,\delta_{\mathrm{C}} = 0 \quad (2)$$

Table 1 Average Values of Various Parameters of the Antarctic Ocean south of the Polar Front

			Reference
Area	2×10^{17} cm^2		16
Precipitation	100 cm yr^{-1}		13
Evaporation	50 cm yr^{-1}		13
Input of continental ice and melt water	5 cm yr^{-1}		14
	10 cm yr^{-1}		15
	S ‰	δ^{18}O‰	
V_{AS}	0	−23	17
V_{CS}	0	−30	17
V_{SA}	0	−4.0	17
V_{SI}	34.00	−0.45	17
V_{SB}	34.65	−0.45	17
V_{DS}	34.74	−0.21	17

where δ_D, δ_S and δ_C are the values for Deep, Surface and Continental melt water respectively, δ_{SB} for the sinking cold water and δ_{AS} and δ_{SA} for the rain-water and evaporative components.

Re-arranging (2)

$$V_{DS}\,\delta_D + V_{AS}\,\delta_{AS} + V_{CS}\,\delta_C = (V_{SI} + V_{SB})\,\delta_S$$

because the surface water goes directly to form AAIW and as freezing has only a very small fractionation effect[17]. Substituting from (1) and re-arranging gives

$$V_{DS} = [V_{AS}(\delta_S - \delta_{AS}) - V_{SA}(\delta_S - \delta_{SA}) + V_{CS}(\delta_{CS} - \delta_C)]/(\delta_D - \delta_S)$$

Evaluating in units of cm yr^{-1} of upwelling

$$V_{DS} = [100\,(-0.45+23) - 50\,(-0.45+4.0) + 10\,(-0.45+30)]/(-0.21+0.45)$$
$$= (2{,}255 - 177.5 + 295.5)/0.24$$

giving $V_{DS} = 9{,}887$ cm yr^{-1}. This is equal to the depth of the mixed layer and represents an average upwelling rate of 63 Sverdrup in excellent agreement with the estimate of Gordon[16]. It follows that the residence time of water in the surface layer is of the order of 1 yr, and certainly between 6 months and 2 yr, because the uncertainty in (δ_D–δ_S) cannot be greater than ±0.1‰. This value for V_{DS} can be used in a salt-balance to estimate V_{SD}. For simplicity

$$S_{AS} = S_{SA} = S_{CS} = 0, \quad S_S = S_{SI}$$

and hence:

$$V_{DS}S_D - V_{SI}S_S - V_{SB}S_{SB} = 0$$

$$V_{SB} = [V_{DS}(S_{DS} - S_S) - (V_{AS} - V_{SA} + V_{CS})S_S]/(S_{SB} - S_S)$$
$$= (7{,}229 - 2{,}040)/(S_{SB} - S_S) = 5{,}189/(S_{SB} - S_S)$$

This is a measure of the removal rate of water whose salinity has been sufficiently modified by freezing that it can sink through the pycnocline. If it is assumed that all sinking occurs in the Weddell Sea, that all the water reaches the bottom and that the mixing ratio with the Deep Water is 1 : 1, then the production rate of Bottom Water is: (5,789/0.65) × 2 = 101 Sverdrup. This is a maximum value which, although in agreement with those of Wust[19] and Le Pichon *et al.*[20], is about three times the value of most other estimates[21]. The important result of these calculations is the very high upwelling rates and correspondingly low residence times found for the surface waters south of the Polar Front.

Sverdrup *et al.*[7] remarked on the striking lateral homogeneity of the Antarctic Circumpolar Current as indicated by sections of T, S and O_2 along its main axis, about 10° south of the Front. In striking contrast the oxygen levels at 2,500 m 15° north of the Front, for instance, are 235 μm kg^{-1} in the South Atlantic and 195 μm kg^{-1} in the South Pacific, the corresponding values for silica being 45 μm kg^{-1} and 100 μm kg^{-1}. The average values in the Circumpolar Deep Water are 210 μm kg^{-1} for oxygen and 110 μm kg^{-1} for silica. From this it can be deduced that there is no simple "source" of Circumpolar Deep Water. Superimposed on the general easterly flow is a southerly component necessary to maintain the upwelling which must occur all around the continent rather than at one or several discrete locations: in addition the rate of entrainment or percentage renewal per circuit must be sufficiently small that the general lateral homogeneity be maintained. Taking the transport south of the Polar Front as 240 Sverdrup (ref. 8) and the upwelling rate as 60 Sverdrup gives the percentage replacement as 25% in the average circuit time of 10 yr, that is an average residence time for water of 40 yr, consistent with the above deductions. While the general composition of the Circumpolar Current is probably controlled by this averaging of the inputs from all round the Southern Ocean, the high silica values suggest that significant chemical processes do occur within the Current itself. Large-scale, light-limited[22] production of diatoms takes place in the nutrient rich upwelled water, leading to significant but highly variable surface depletions of dissolved silica. Edmond and Jacobs (unpublished data) found a range of from less than 10 to over 80 μm kg^{-1} on Eltanin 47 (January to April 1971). Taking the average concentration of silica in the incoming water as 70 μm kg^{-1}, and in the Deep Water as 110 μm kg^{-1}, then with the 40 yr residence time an input of silica of 7.2×10^{19} μm yr^{-1} is required to maintain the Deep Water levels (mean thickness of the Deep Water taken as 3,600 m).

The published Eltanin data[23,24] suggests an average silica concentration in the mixed layer of 60 μm kg^{-1}. If the depletion occurs by stripping of the mixed layer by diatoms then the input is 10^{20} μm yr^{-1} (100 m mixed layer, residence time of 1 yr). This is sufficient to maintain both the high silica concentrations in the water column and the high sedimentation rate of diatoms all around the continent. Even these very crude calculations show clearly that the Antarctic diatomites represent a net sink for silica and that no local injection is required in order to maintain the steady state situation: a massive source of silica from glacial sediments is ruled out.

The now-classic problem posed by Sillèn[25] concerning the equilibrium versus steady-state control of the silica and other cycles in the ocean is very difficult to answer directly. The stream supply of silica is estimated by Livingston[26] at 4.3×10^{14} g SiO_2 yr^{-1} corresponding to 7.2×10^{18} μm Si yr^{-1}. This is a factor of ten less than the estimated dissolution rate of diatomaceous opal in the Circumpolar Current. Bacon and Edmond[27] estimate the total dissolution rate of opaline silica at 4.4×10^{18} g Si 10^{-3} yr corresponding to 1.6×10^{20} μm Si yr^{-1}. We see that the net fluxes into and out of the oceanic reservoir of dissolved silica are very small compared to the internal fluxes of precipitation and dissolution of opal. The cyclic processes dominate over the primary ones. It is therefore not feasible to attempt to identify net fluxes of silica into various reservoirs by mass balance calculations.

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Equilibrium Cross-section of Meandering and Braided Rivers

THERE are two simple models which describe the equilibrium state of a channel cross-section with constant conditions, one static, the other dynamic. In the first case equilibrium is said to hold when all grains on the bed are just at the threshold of movement[1]. Because movement is produced by a combination of fluid drag and the downslope gravity component and because the fluid drag is greatest in the centre of the channel, the channel slopes can increase up the sides to compensate for the decrease in drag. The resulting profile is roughly a parabola[1] and is very similar to many natural channel forms. This static model is particularly relevant to the design of some canals where discharges are fairly constant and the bed material is normally immobile. Natural rivers transport sediment, however, and the mean channel form develops at high stages when nearly all the bed material is in intermittent motion. When sediment is transported as bed load it must be continually tending to creep downslope into the centre of the channel under the influence of gravity. If, however, the channel maintains a constant profile there must be an equal and opposite tendency at all points for the sediment to move sideways upslope. Apart from buoyant upthrust, the only other force acting on the grains is the fluid drag acting in the direction of the water flow, leading to the second model. When river channels are in dynamic equilibrium the flow along the bed has a sideways component up the channel banks which exactly compensates the tendency of the sediment to move downslope under the influence of gravity. As water flowing sideways along the bed must return to the channel centre along the surface this implies that the river has a double spiral secondary flow (Fig. 1). Although double spiral flow in straight channels has been demonstrated[2,3], single spiral flow in meander bends is better known[1]. As, however, the sense of the spiral changes from one bend to the next, it follows from considerations of continuity and symmetry that in the straight reaches between bends there is a transitional double spiral structure (Fig. 1 *C*). In short the secondary flow in river channels is a double spiral which is asymmetrically developed in bends so that one vortex momentarily excludes the other at the crest of the meander. The two spirals adjoin where the flow attaches itself to the bed and diverges sideways; this line is also the thalweg or deepest part of the channel. It is no coincidence that the same hypothesis of double spiral flow is commonly used to explain the origin of many sand ridge bed configurations formed parallel to the flow, such as primary current lineation, sand ribbons, tidal current ridges and longitudinal aeolian dunes and draas[4,5]. River channels are analogous to the troughs between longitudinal sand ridges in certain other respects too: they arise spontaneously during sediment transport, reach a dynamic equilibrium by interaction with the flow and are associated with transverse structures, forming meander bars, that migrate downstream. In short, there is a good case for saying that the entire form of a river channel is a bed configuration *sensu stricto*.

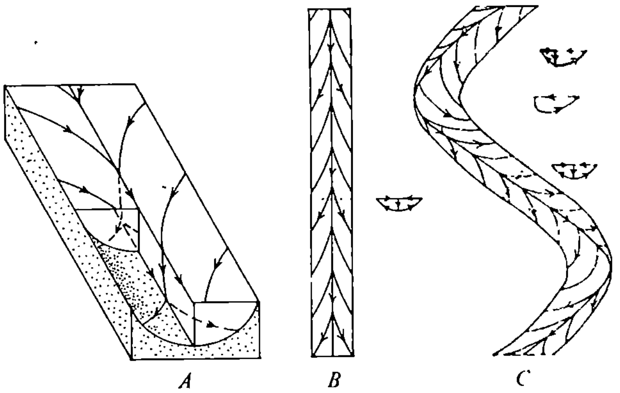

Fig. 1 Models for double spiral flow in channels. *A*, *B*, Symmetrical double spiral. In nature this is found at the cross-over on the straight reaches. *C*, Asymmetrical double spiral in a meandering channel. The pitch of the spiral is exaggerated to make the relations clearer.

The long profile of a river changes slowly with the passage of time or in response to changes in climate or base level. In contrast the cross-sections of river channels change rapidly in response to changing conditions, particularly varying discharge. This is understandable because in the first case large quantities of material have to be moved hundreds of kilometres downstream, and in the second case only small quantities are involved and they need only be moved hundreds of metres laterally. The cross-section of a river tends to grow towards a constant equilibrium profile. Because the flow conditions in all rivers fluctuate rather rapidly such an equilibrium is never reached; however, it is quite sensible to consider the mean cross-profile of many rivers as being in an approximate equilibrium with the mean flow conditions. This is rarely true if they are cut in and restricted by bedrock, but it is probably true of most rivers flowing in unconsolidated alluvium. Furthermore, since the cross-profile adjusts much more rapidly than the long profile to changing conditions, the effect of changes in long profile in upsetting the mean equilibrium cross-section can be considered as negligible. All unrestricted channel thalwegs, whether in single or multichannel streams, have a tendency to be sinuous[6]. This sinuosity also tends to reach an equilibrium form dependent on the conditions and it also adjusts to changes in these much more rapidly than the long profile. Here I discuss only the mean channel cross-section and I make the simplifying assumption that the sinuosities are averaged out to form a single symmetrical straight channel.

Consider a river channel in equilibrium. At every point the downslope gravity component acting on a moving grain is balanced by the upslope component of the fluid drag, both forces acting normal to the channel axis. In given flow conditions, the forces acting on a single grain in a bed of mean grain diameter d are related to its size by

$$\text{Gravity component} \propto d^3$$
$$\text{Fluid drag component} \propto d^2$$

because the former is a body force and the latter a surface force. Consider exactly the same situation where the grain size is

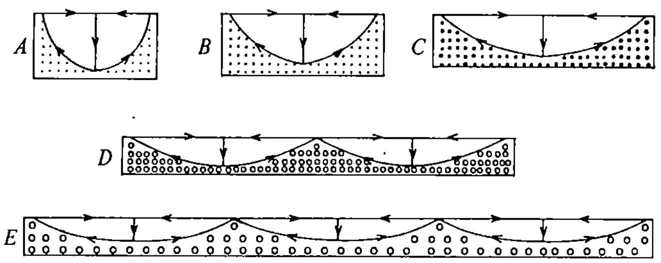

Fig. 2 Hypothetical differences in the equilibrium cross-profiles of rivers with the same slope and discharge but different bed grain sizes (increasing from *A* to *E*).

doubled. Neglecting the effect of the small change in bed roughness, the fluid drag per unit area remains the same and the upslope fluid drag on each grain is increased four-fold. However, the downslope gravity component per grain is increased eight-fold. This means that the profile is no longer in equilibrium and the grains move inwards from the sides to the centre of the channel, making the cross-section wider and shallower. As the side slopes become gentler the downslope component decreases until a new equilibrium is reached. If the grain size were halved instead of doubled the upslope fluid drag on each grain would be reduced to a quarter and the downslope force reduced to an eighth. In this case the lateral component of spiral flow would move sediment from the centre up the sides of the channel until a new equilibrium had been reached with a narrower, deeper, steeper sided cross-section. This shows that, other things being equal, rivers with coarse grained beds are wide and shallow and rivers with fine grained beds are narrow and deep (Fig. 2). An important corollary of this is that the coarsest material gravitates to the centre of the channel, not because the fluid drag is greater there but because the side slopes are gentler.

As the channel changes so must the shape of the spiral vortex within it. This accommodation is unlikely to continue indefinitely, however, because the secondary flow has its origin in hydrodynamic instability and the causal factors involved do not include the forces acting on individual sediment grains. In fact, the occurrence of the spiral flow is probably independent of whether the bed is fixed or mobile and of whether the water is restricted to a channel or flows in a wide sheet. It would be reasonable to expect the width of unrestricted spiral vortices to increase with deepening water and *vice versa*, because the dimensions of natural entities usually increase or decrease together even if their relative proportions do not remain the same. If the water depth is decreased with constant width or the width increased with constant depth, sooner or later the secondary flow will break up into two and subsequently many spiral pairs. This has been demonstrated experimentally[6-8]. Each of these spiral secondary flow systems should form a sub-channel in the river. The foregoing argument suggests that a change of grain size affects the equilibrium cross-profile of a river in the way shown in Fig. 2. With increasing grain size the channel becomes shallower and wider until a stage is reached where the secondary flow divides to form two vortex pairs with two sub-channels and subsequently many vortex pairs with many sub-channels. This hypothesis explains the origin of braided multichannel rivers. Other things being equal, braided rivers will form with coarse grained beds and meandering rivers with fine grained ones.

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The Racemization Reaction of Isoleucine used as a Palaeotemperature Indicator

IT has been shown that the slow racemization reaction of amino-acids can be used in geochronology[1-4]. One reaction of particular interest is that involving isoleucine. The racemization of L-isoleucine (iso) produces the non-protein amino-acid D-alloisoleucine (alleu), and these two can be separated on an automatic amino-acid analyser. The isoleucine racemization reaction in bone has a half-life at 20° C in excess of 100,000 years and preliminary evidence suggests that the reaction can be used to date fossil bones too old to be dated by radiocarbon[4].

The ages based on the racemization of isoleucine are calculated from the equation (see refs. 3 and 4 for derivation):

$$\text{“age” (years)} = \frac{\text{Ln}\left[\dfrac{1+(\text{alleu/iso})}{1-0.725\ (\text{alleu/iso})}\right] - 0.028}{(1.725)(10^{19\cdot 41-7304\cdot 0/T})} \qquad (1)$$

where T is the average temperature (K) of the bone since deposition. It is evident from this equation that because of the sensitivity of the racemization reaction to temperature, some estimate of the temperature history of the sample must be available. Conversely, if the age of a bone can be determined by an alternative method, the racemization reaction can be used to calculate the average temperature which a bone has experienced since it was deposited. Thus, under certain conditions, the racemization reaction could be used as a palaeothermometer; we now describe an example of such a use of the reaction.

We analysed samples from the site of Florisbad, near Bloemfontein, Orange Free State, South Africa. The bones were from a peat layer (Peat I) which was next to the "eye" of a warm lithium spring. Peat I is the lowest of several peat layers and contained hominid and faunal remains and several wooden implements.

The bones used in these investigations were from an extinct hippopotamus (*Hippopotamus amphibus*). Radiocarbon analysis of the collagen fraction isolated from a mandible yielded an age of 38,680±2,000 yr (UCLA-1745B); the radiocarbon age of a wooden implement associated with the jaw bone was determined to be 38,550±3,800 yr (UCLA-1745C). In 1932 the fragmentary skull (facio-calvarial fragments) of *Homo* (*Africanthropus*) *helmei* was recovered from the Florisbad site[5]. These hominid remains can now be dated by the radiocarbon ages of the hippopotamus and wooden implements. Organic matter from the peat was used by several laboratories to date this site[6-9]; our dates are the first on individual fossil or cultural materials. The archaeological and anthropological implications of the new radiocarbon ages are discussed elsewhere[10].

Amino-acid analyses were carried out on a piece of the hippopotamus jaw bone and also on a portion of a tooth associated with the jaw. The samples were processed and analysed according to the procedure described elsewhere[4]. We found the alleu/iso ratios to be 0.46 (bone) and 0.42 (tooth).

Substituting these ratios and the radiocarbon age into equation (1) yields a temperature of $26.5 \pm 0.3°$ C. The present average temperature in the spring is about 28° C (private communication from H. Oberholzer), which agrees well with the value deduced from the isoleucine racemization reaction. Moreover, because the analysed materials were not from the spring itself, but were from the adjacent peat layer, the calculated and actual temperatures of the samples are probably even in closer agreement.

It should be emphasized that a temperature calculated from the amino-acid racemization reaction is the average temperature to which the bone has been exposed. The fact that the calculated temperature of $\sim 27°$ C for the spring so closely matches its present temperature suggests that there have been no large scale temperature fluctuations of long duration; the spring temperature has apparently been nearly constant for a period of at least 40,000 yr. By contrast, because of temperature variations during glacial periods, the average temperature for the surface waters of the tropical Atlantic Ocean during the past 40,000 years is $\sim 24°$ C, almost 3° C lower than the present ocean temperature[11]. It has also been estimated[2], from the oxygen isotopic composition of two speleotherms, that the inland regions of New Zealand have experienced a similar lower average temperature during the past 40,000 yr. This 3° C decrease in average temperature is not seen in the Florisbad warm spring. Either the spring temperature has been unaffected by climatic variations in the surrounding environment or, during the past 40,000 years, the temperature fluctuations in South Africa were much smaller than elsewhere on the Earth.

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BIOLOGICAL SCIENCES

The Unexpected Location of a Gene conferring Abnormal Radiation Sensitivity on Phage T4

THREE mutations have been characterized, each of which increases the radiation sensitivity of phage T4 by a factor of about two. The *v* gene, controlling excision repair, maps close to gene *1* which codes for hydroxymethyl-dCMP kinase, a precursor of phage DNA synthesis[1-3]. The *x* gene, which probably is involved in a post-replication repair system, maps close to gene *43*, the gene coding for the phage Kornberg polymerase[1,3,4]. The third gene, *y*, affects radiation sensitivity in a similar manner to *x*[5]. It has not previously been mapped, although it has been shown to be unlinked both to *v* and to *x*[4]. We have now located the *y* gene on the circular genetic map of phage T4. Unlike *v* and *x* which as expected map close to known early genes involved in phage DNA synthesis, the *y* gene is surrounded by late genes which determine the structure and assembly of the phage head and tail (Fig. 1).

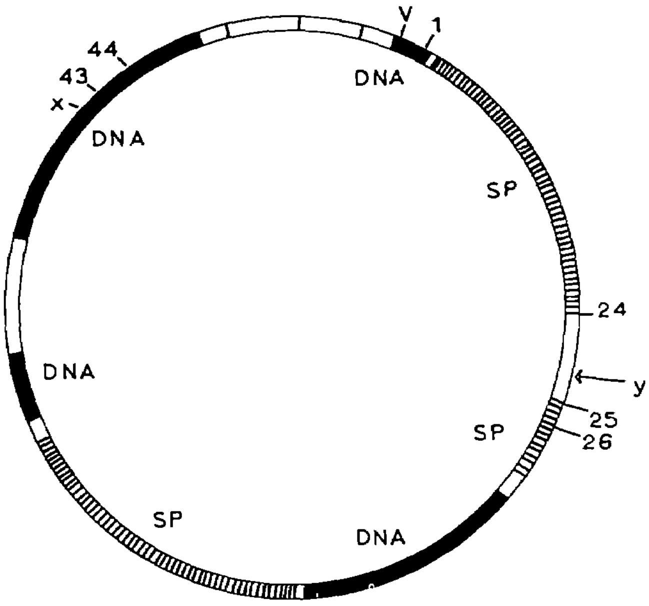

Fig. 1 Simplified circular genetic map of phage T4 (after Edgar and Wood[6]) showing the locations of the genes mentioned in the text. Genes known to affect DNA synthesis all lie in the portions of the genome marked "DNA". With very few exceptions, genes known to be involved in the synthesis and assembly of phage structural proteins lie in the portions marked "SP".

The original *y* mutant was isolated from a phage stock which had been heavily mutagenized with hydroxylamine, and then back-crossed four times with T4 wild-type. The resultant phage variant, called y_{10}, showed an amber phenotype in that its ultraviolet sensitivity was normal when assayed on su^+ bacteria but was enhanced when assayed on su^- bacteria; however, it plated equally well on both types of bacterial strain. On performing further back-crosses with y_{10} we observed a great heterogeneity in the plaque-types among the phage lysates suggesting that y_{10} was still a multiple mutant. After a further series of back-crosses we finally isolated a phage variant, termed y_{100}, which now behaved like an essential amber mutant having an efficiency of plating of less than 10^{-3} on su^- bacteria as compared to its titre on su^+ hosts. The rare plaques arising from y_{100} when plated on su^- bacteria were shown to be due to pseudo-revertants which now had the same radiation properties as y_{10} and genetically could be analysed as double-mutants containing y_{100} coupled with suppressor mutations which map at a number of sites on the T4 genome.

Having now isolated as an essential amber mutation the ingredient in y_{10} which determined its radiation sensitive properties, it was comparatively straightforward to map y_{100} by conventional 2-factor crosses with known amber mutants. This procedure gave no indication of linkage between y_{100} and genes in the known early regions of the genome but did indicate a definite linkage with the late genes *24*, *25* and *26*, recombination frequencies being 18%, 8% and 12% respectively. To locate the y_{100} mutation more accurately with regard to these genes a series of 3-factor crosses of the type $am24\text{–}y_{100} \times am25$ was performed. All the plaques obtained by plating the progeny on su^+ indicator were then analysed and the ratio of y^+/y phage determined among the am^+ recombinants. The results are presented in Table 1, together with those of a 2-factor cross between y_{100} and *am*25 analysed in the same non-selective manner. The only interpretation of these results which is consistent with the observation that the mutations used in genes *25* and *26* are about 8 map units apart is that the *y* gene lies between genes *24* and *25*.

Table 1 Non-selective Analysis of 2 and 3 Factor Crosses of the Type $am \times y$ and $am\text{-}y \times am$

Type of cross	Total	Plaques scored am^+y^+	am^+y	am^+y^+/am^+y
$24y \times 25$	1,078	15	112	0.13
$24 \times 25y$	1,006	128	26	4.92
$25y \times 26$	1,527	75	16	4.69
$25 \times 26y$	1,419	11	53	0.21
				Recombination frequency
$25 \times y$	1,072	41		7.6

The amber mutants used were B26 (gene *24*), N67 (gene *25*) and N131 (gene *26*). Crosses were carried out in su^+ host bacteria and the progeny then plated, also on su^+ bacteria. In the 3-factor crosses individual progeny plaques were first tested by complementation against the appropriate double amber mutant, and the *y* phenotype of all am^+ recombinants was identified by examining both their relative plating efficiencies and ultraviolet sensitivities on su^+ and su^- indicator. A similar procedure was employed in analysing the 2-factor cross.

The present results are of interest for two reasons. First, they have identified a new essential gene in phage T4 which, because it is implicated in radiation repair, is presumably involved in some aspect of phage DNA synthesis. Second, they suggest that the previously uncharted region of the T4 genome which lies between genes *24* and *25* (and is approximately 20 map units in length) represents a further region which contains genes involved in early functions.

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Thymus and Bone Marrow Derived Lymphatic Leukaemia in Mice

VERY little information is available concerning the origin of the lymphoid cells of human and animal leukaemias. The lymphoid cell population has been divided into two different functional groups, namely the thymus derived lymphocytes (T cells) mainly involved in cell mediated immunity, and the bone marrow derived lymphocytes (B cells) mediating humoral immunity. These two lymphocyte categories have not been distinguished morphologically, but several specific markers for their identification have been described. The thymus, brain and thymus derived lymphocytes (T cells) bear a cell surface isoantigen θ[1] and have very little detectable immunoglobulin molecules on their surface; whereas the bone marrow derived lymphocytes (B cells) have a high density of immunoglobulin determinants on their surface[2].

Several examples of B lymphocyte leukaemias have been reported. Among human leukaemias and lymphomas several cases of chronic lymphatic leukaemia[3–5] and Burkitt lymphoma[6] were described as having surface immunoglobulins on the lymphocyte cell membrane, therefore representing a B-lymphocyte malignancy. Similarly, a cell passage line of a spontaneous occurring leukaemia in guinea-pigs was shown to have multiple properties characteristic of bone marrow derived B cell population[7].

It has been established that radiation and virus induced lymphatic leukaemia in mice are usually dependent on the presence of the thymus which is probably the target organ for the actual neoplastic transformation[8]. By contrast, we found that the induction of lymphatic leukaemia in the inbred SJL/J strain of mice by a chemical carcinogen was not thymus dependent, as we obtained a high incidence of lymphatic leukaemia in thymectomized mice treated with the carcinogen[9]. We thought it of interest to analyse the lymphocyte origin of radiation, virus and chemical carcinogen induced lymphatic leukaemias and lymphosarcomas.

We chose for these studies the SJL/J strain of mice which were previously shown to be susceptible to lymphatic leukaemia induction by chemical carcinogens, fractionated irradiation, or by a virus isolated from isogenic irradiated non-leukaemic bone marrow[9,10]. Our first attempt was to induce lymphatic leukaemia by a chemical carcinogen in mice devoid of T cells. It has been shown that injection of isologous bone marrow to thymectomized irradiated adult mice prevents thymus derived lymphocyte differentiation from the injected bone marrow, and bone marrow derived lymphocytes persist as the predominant lymphocytes in the lymphoid tissues[11]. This method was used to obtain SJL/J mice with a bone marrow derived lymphocyte population in their lymphoid tissues. The carcinogen 7,12-dimethylbenz(a)anthracene (DMBA) was used for tumour induction. The carcinogen was made up as a 1% solution in polyethylene glycol 400 and administered to the mice four times at weekly intervals by stomach tube prepared from polyethylene tubing of about 1 mm bore size. A dose of 1 ml. of the DMBA solution (1 mg DMBA) was given at each feeding.

Five week old female SJL/J mice were thymectomized and thereafter divided into three groups. One group was treated with DMBA, starting 6 weeks after thymectomy was performed in these mice. Thymectomized mice of the second group were exposed to 550 R whole body irradiation and 2 weeks thereafter treated with DMBA. The third group was exposed 4 weeks after thymectomy to 800 rad whole body irradiation and within 1 h after irradiation they were reconstituted with 10^6 isologous normal bone marrow cells and two weeks later treated with DMBA. The leukaemogenic potency of DMBA treatment was also evaluated in intact female SJL/J mice treated with carcinogen when 11 weeks old. Lymphatic leukaemia developed in all the different treated groups, the incidence ranging between 52–70% at an average latent period of 130–160 days (Table 1). A low incidence of stem cell leukaemia,

Table 1 Lymphatic Leukaemia Induction in SJL/J Mice by 7,12-Dimethylbenz(a)anthracene (DMBA)

Treatment of host	Lymphatic leukaemia incidence	Stem cell leukaemia incidence	Myeloid leukaemia incidence	Reticulum cell sarcoma incidence
Thx* $\xrightarrow{\text{6 weeks}}$ DMBA × 4	14/27–52% (160)	4/27–15% (136)	1/27–3.7% (170)	7/27–26% (242)
Thx $\xrightarrow{\text{4 weeks}}$ 550 R W B $\xrightarrow{\text{†2 weeks}}$ DMBA × 4	23/33–70% (142)	3/33–9% (156)	2/33–6% (110)	4/33–12% (270)
Thx $\xrightarrow{\text{4 weeks}}$ 800 R W B $\xrightarrow{\text{1 hour}}$ BM $\xrightarrow{\text{‡ 2 weeks}}$ DMBA × 4	12/20–60% (132)	4/20–20% (160)	1/20–5% (140)	1/20–5% (170)
Intact $\xrightarrow{\text{11 weeks}}$ DMBA × 4	15/28–52% (154)	4/28–14% (174)		5/28–18% (213)

Female SJL/J mice were thymectomized at the age of 5 weeks. DMBA treatment: four feedings of 1 mg in polyethylene glycol 400 administered by stomach tube at weekly intervals.

The average latent period in days is given in parentheses.

* Thymectomy. † Whole body irradiation. ‡ 10^6 isologous normal bone marrow cells injected intravenously.

myeloid leukaemia and spontaneous reticulum cell sarcoma was also observed (Table 1). This demonstrated the ability to induce lymphatic leukaemia by a chemical carcinogen in mice devoid of thymus derived lymphocytes, namely leukaemias that originate from a bone marrow derived population of lymphocytes.

Thymus dependent lymphatic leukaemia was induced by irradiation or by a leukaemogenic virus. Five week old SJL/J mice were exposed to four weekly doses of 170 R whole body irradiation. Thymic lymphomas occurred in 40% of the irradiated mice at an average latent period of 200 days.

The leukaemogenic virus used in the studies for thymic lymphoid leukaemia induction was prepared from thymic lymphoid leukaemias induced in SJL/J mice by live serial passage of the virus originally isolated from irradiated non-leukaemic bone marrow as previously described[10,12]. The cell free extract (0.02 ml.) was injected directly into the adult thymus, and 2 days later the inoculated mice were exposed to 400 R whole-body irradiation[13]. Thymic lymphoid leukaemia developed in 70% of the inoculated mice at an average latent period of 150 days.

The markers which characterize T and B cells were used to identify the lymphocyte origin of the above mentioned induced lymphatic leukaemias. The detection of the θ antigen, which is present on the bulk of thymus lymphocytes and on thymus derived lymphocytes, served to establish the percentage of thymus derived lymphocytes in the various induced leukaemias. The evaluation of θ bearing leukaemic cells[1] was carried out on cell suspensions from DMBA, radiation or virus induced leukaemias (cells taken from primary tumours or from first to third cell passage material) as well as on thymus and lymph node cells taken from 2 month old normal SJL/J mice. Anti θ C_3H serum was prepared according to the method of Reif and Allen[14]. Two month old AKR mice were immunized with C_3H/eb thymocytes; 10×10^6 thymocytes were injected intraperitoneally at weekly intervals for 7 weeks. The mice were bled one week after the last thymocyte inoculation. Each serum preparation was titrated against normal mouse thymocytes; in most cases it was diluted 1:4 with saline. Normal AKR serum was used as control. Cell suspensions of various leukaemias and normal thymus were prepared in cold in minimal 'Eagle's medium' (MEM) containing 0.1% BSA. The suspensions were washed twice and adjusted to $5\text{–}10 \times 10^6$ cells ml.^{-1}. To 0.1 ml. of cell suspension, 0.1 ml. of anti C_3H serum was added. The mixture was incubated for 15 min at 37° C. After washing once with MEM—BSA, 0.1 ml. of guinea-pig complement was added and the mixture was incubated for another 30 min at 37° C. Cytotoxicity was estimated by the dye exclusion of trypan blue in saline. The controls used were cells in normal AKR serum (1/4); cells in antiserum without complement. The θ antigen was detected in 70% of the lymphocytes taken from radiation or virus induced leukaemias. In contrast only 15% of the lymphocytes from leukaemias induced in intact mice treated with DMBA carried θ antigen and 4.3% of lymphocytes obtained from thymectomized irradiated DMBA treated leukaemia mice (Table 2).

Table 2 Surface Antigens in DMBA, Radiation and Virus Induced Lymphatic Leukaemia in SJL/J Mice

Type of cell tested	No. of mice	Mean % θ bearing lymphocytes	IgG, IgM immuno-globulins
DMBA induced leukaemia in intact mice	10	15% (0–35%)	+ + + +
DMBA induced leukaemia in thymectomized irradiated mice	7	4.3% (0–14%)	+ + + +
Virus induced leukaemia	7	70% (58–88%)	− − − ±
Radiation induced leukaemia	5	75% (62–87%)	− − − −
Normal thymus	5	77% (66–85%)	− − − −
Normal lymph nodes	3	27% (25–30%)	+ +

2 month old female SJL/J mice were used. DMBA treatment: four feedings at weekly intervals of 1 mg in polyethylene glycol 400. Virus induced lymphatic leukaemia: 0.02 ml. of the cell free extract was injected directly into one thymus lobe of the mouse, which was further exposed 2 days later to 400 R whole body irradiation. Radiation induced lymphatic leukaemia: four doses of 170 R whole body irradiation at weekly intervals.

Immunoglobulin determinants on the surface of lymphoid cells were detected using the direct immunofluorescent technique[2,15]. Living cells from the different induced leukaemias were washed in PBS containing 1% gelatin and then exposed to fluorescein conjugated anti-mouse immunoglobulin reagents (anti IgG and anti IgM). After incubation for 30 min at 37° C the cells were washed three times in PBS-1% gelatin and resuspended in 50% glycerin and stored at 4° C. As the cells were alive during the procedure the antibodies could only react with cell surface immunoglobulins. Surface staining was found only in lymphocytes from DMBA induced leukaemias (Table 2). The intensity and distribution of the staining were similar among the leukaemic lymphocytes taken from intact or thymectomized irradiated hosts treated with DMBA. It had a striking distribution and many of the labelled cells showed a defined fluorescent "cap" at the cell surface.

Thus the DMBA induced lymphatic leukaemia in intact or thymectomized irradiated hosts appeared to be of B lymphocyte origin whereas the radiation and virus induced lymphatic leukaemia was of T lymphocyte origin. These findings are not specific for the SJL/J strain of mice. Preliminary studies in our laboratory concerned with the lymphocyte origin in lymphatic leukaemia induced in the C57BL and C_3H strains of mice indicate that radiation and virus induced leukaemia in these strains of mice were also of T lymphocyte origin, whereas all DMBA induced leukaemias so far tested were found to be derived from bone marrow lymphocytes.. Our results differ from those obtained by Shevach *et al.*[16], who analysed 21 mouse leukaemias, including some chemical carcinogen induced cell lines, and found that none of them could be classified as B lymphocyte leukaemias.

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Co-carcinogenic Effect of Progesterone on 20-Methylcholanthrene Induced Cervical Carcinoma in Mice

THE secretion of mucosubstances in the genital tract seems to be related to the ovarian output. It is well known that ambivalent cells of the vaginal squamous epithelium keratinize under oestrogenic action and mucify when progesterone acts synergically with oestrogen. This last condition seems to be required, at pro-oestrus, a few hours before ovulation. Direct evidence of oestrogen secretion at early pro-oestrus[1,2] and of progestin surge at mid-pro-oestrus in mice[3] and in rats[4] has been demonstrated.

At pro-oestrus, however, mucosubstances appeared in the cells of the genital tract of control C57BL6 mice. In this experiment we have shown that these mucosubstances were histochemically different. Acid and carboxyl mucosubstances were secreted by vagina and exocervix, but the uterine columnar epithelium secreted neutral mucosubstances, while the endocervical mucosal epithelium did not produce any glucidic secretion. In the course of this study, mucosubstances were systematically looked for in the squamous epithelium and were shown by the following histochemical reactions: PAS, salivary amylase, alcian blue (*p*H 2.6 and 1).

Progesterone administered for 9 weeks by subcutaneous implantation of pellets with a dose of 15 mg/mouse/3 weeks, to 25 C57BL6 3-month-old mice induced a strong intracellular reaction of mucification along the vaginal mucosa to exocervix. In the endocervical squamous epithelium, acid and carboxyl mucosubstances appeared only in few foci of cells. As, however, no glucidic secretion was exhibited in the endocervical cells during the normal oestrous cycle, it can be concluded that parenteral administration of progesterone induced a mucin-producing metaplasia in the endocervical mucosa.

Local exposure of carcinogen, 20-methylcholanthrene (MC), in the cervical canal for 9 weeks, in 50 C57BL6 3-month-old mice induced one invasive carcinoma in the vagina–exocervix and five in the endocervix.

Parenteral administration of progesterone to 50 C57BL6 mice for 9 weeks at the dose mentioned above was associated with carcinogenic action and significantly increased the total number of invasive squamous carcinoma in vagina–exocervix and in endocervix, as shown in Table 1.

Table 1 Histological Types of Invasive Squamous Cell Carcinoma Appearing in the Vagina–Exocervix and Endocervix after Local Application of 20-Methylcholanthrene (MC) with and without Progesterone (P) after 9 Weeks Treatment

	Vagina–exocervix			Endocervix		
Invasive squamous cell carcinoma	MC	MC+ P	*P* value	MC	MC+ P	*P* value
Immature microcarcinoma	0	9	0.01	3	9	n.s.
Keratinized	0	1	n.s.	1	0	n.s.
Mucin-secreting	1	5	n.s.	1	21	0.01
Total number of invasive squamous cell carcinoma	1	15	0.01	5	30	0.01

Histochemical and histological examination of a hundred specimens under study showed that in our experimental conditions progesterone selectively influenced the maturation of the induced endocervical invasive carcinoma, gave a mucoepidermoid type ($P < 0.01$) and had no effect on the maturation of induced invasive carcinoma from the vagina and the exocervix which remained immature.

Our results would indicate that endocervix in the strain of mice used might be a target organ for the action of progesterone or for its metabolites.

The progestative hormone, by inducing a mucin-secreting metaplasia in the target organ, could make it sensitive to the action of the carcinogen, and would thus influence the histological type of the induced carcinoma. The role of progesterone on the carcinogenesis of the cervix has received very little attention[5,6]. Kaminetzky[7] noted that progesterone administration advanced cervical dysplasia induced by 20-methylcholanthrene and Glücksmann and Cherry[8] drew attention to the fact that progesterone treatment did not affect the total number of induced tumours but increased the incidence of adenocarcinoma secreting mucus. Our findings suggest the possibility that a prolonged and high dose of progesterone or progestins which are known to provoke a strong stimulation of human endocervical glands[9,10] could promote carcinogenic activity of the agent primarily responsible for cervical tumours in women and tend to favour selectively the development of the mucoepidermoid maturation of the cancerous cells.

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Cholera Enterotoxin: Failure of Anti-inflammatory Agents to Prevent Cyclic AMP Accumulation

THERE is considerable evidence that cholera diarrhoea is caused by accumulation of cyclic AMP in intestinal mucosa, stimulated by cholera enterotoxin[1–3]. Prostaglandin-E_1 (PGE_1) reproduces the effects of cholera enterotoxin on both cyclic AMP and secretion of fluid and electrolytes by intestinal mucosa[3] and it was suggested[4] that the toxin might first act by stimulating the release or synthesis of prostaglandin which then acts through cyclic AMP. Bennett[4] proposed that acidic anti-inflammatory drugs, as they are potent inhibitors of prostaglandin synthesis in several tissues[5–7], might antagonize the effect of cholera enterotoxin. Jacoby and Marshall reported that indomethacin, aspirin, and several other anti-inflammatory agents inhibited the cholera toxin-induced accumulation of fluid in ileal-ligated rats[8]. Because of its potential therapeutic significance, I have studied this proposed mechanism.

The cyclic AMP system is stimulated by cholera enterotoxin in virtually every tissue so far tested, including liver, adipose tissue, and blood platelets, in addition to intestinal mucosa[1,9–11]. Low concentrations (1–10 ng ml.$^{-1}$) of the purified toxin increased adenyl cyclase activity and cyclic AMP accumulation in human leucocytes[12,13], and this effect was similar in all respects to that on intestinal mucosa, including toxin concentration required, the characteristically delayed time-course, and specific inhibition by cholera toxoid and a canine antitoxin. The leucocyte seemed a suitable tissue for testing Bennett's suggestion *in vitro*, as PGE_1 also stimulates leucocyte cyclic AMP accumulation[13–15].

Leucocytes of three healthy human volunteers were prepared as described previously and suspended in a Tris-buffered salt solution containing 0.3% (w/v) human serum albumin[14]. Leucocytes (1×10^7 ml.$^{-1}$) and purified cholera enterotoxin 10 ng ml.$^{-1}$, a maximally effective concentration[12]) were incubated for 90 min at 37° C. Varying concentrations of indomethacin or aspirin were added to leucocytes 5 min before addition of cholera toxin. Incubation was terminated by centrifugation (2,000*g* for 1 min), after which the supernatant fluid was discarded and the cell button resuspended in ice-cold 5% trichloroacetic acid. Leucocyte cyclic AMP was then assayed by the competition-binding method of Gilman[16], modified as described previously[15].

Table 1 Leucocyte Cyclic AMP after Exposure to Anti-inflammatory Agents and Cholera Enterotoxin

	Cyclic AMP, picomol per 10^7 cells *		
	Exp. 1	Exp. 2	Exp. 3
No drug	4.4	7.2	5.6
Indomethacin 70 µg ml.$^{-1}$	5.0	10	7.4
Aspirin 700 µg ml.$^{-1}$	—	9.0	8.0
Cholera enterotoxin 10 ng ml.$^{-1}$	39	75	45
+Indomethacin 70 µg ml.$^{-1}$	41	84	44
+Indomethacin 7 µg ml.$^{-1}$	38	69	43
+Indomethacin 0.7 µg ml.$^{-1}$	37	72	44
+Aspirin 700 µg ml.$^{-1}$	—	76	39
+Aspirin 70 µg ml.$^{-1}$	—	73	40
+Aspirin 7 µg ml.$^{-1}$	—	67	43
+Aspirin 0.7 µg ml.$^{-1}$	—	68	42
PGE_1 1×10^{-5} M	32	50	40

* Each value is the mean of duplicates differing by ±8%.

Neither aspirin nor indomethacin produced any detectable inhibition of the eight-fold increase in leucocyte cyclic AMP caused by cholera enterotoxin (Table 1). PGE_1 alone caused accumulation of cyclic AMP, as described previously[13–15]. The maximal concentrations of both anti-inflammatory agents were considerably higher than those which produced complete inhibition of prostaglandin synthesis in guinea-pig lung[5] and canine spleen[7]; 3–4 µg ml.$^{-1}$ for indomethacin and 30–40 µg ml.$^{-1}$ for aspirin.

The similarities between cholera enterotoxin's effects on the cyclic AMP content of gut mucosa and leucocytes suggest that the toxin's mechanism of action may be similar in the two tissues. If so, high concentrations of aspirin and indomethacin would not be expected to prevent accumulation of cyclic AMP in gut mucosa exposed to maximally effective doses of cholera enterotoxin. This possibility must be tested directly with maximally—and submaximally-effective doses of cholera toxin on the gut mucosa, and it must be shown in both leucocytes and mucosa that indomethacin and aspirin greatly reduce prostaglandin synthesis The present results show that cholera toxin alone can increase cyclic AMP levels maximally in human leucocytes. They do not exclude the possibility that the gut behaves differently or that a dual mechanism exists. In addition to the direct action of toxin there might be an indirect effect involving prostaglandins, and this would become evident only in experiments with the submaximal doses of toxin. Nevertheless, increased synthesis of prostaglandin is unlikely to prove a universal mechanism for the actions of cholera enterotoxin, since the toxin (like cyclic AMP) stimulates lipolysis in adipocytes[9], cells in which PGE_1 inhibits both cyclic AMP accumulation and lipolysis[17,18].

These results do not preclude a beneficial therapeutic effect of acidic anti-inflammatory agents in cholera. The inhibition of toxin-induced intestinal fluid accumulation by these agents *in vivo*[8] deserves further investigation, even if it belongs to a class of drug effects in which cyclic AMP plays no role.

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Development of K^+-Conductance and Membrane Potentials in Unfertilized Sea Urchin Eggs after Exposure to NH_4OH

THE fertilization of the sea urchin egg starts a sequence of changes in the cell membrane which can be measured as changes of membrane potential and membrane resistance[1-3]. The immediate consequence of contact of ovum and spermatozoon is an action potential, a depolarization and repolarization including a transient reversal of polarity. The overall sequence[1,2] converts the anion-permeable membrane of the unfertilized egg (with a potential of about −10 mV, inside negative) to a rather typical K^+ permeable membrane (about −60 mV, inside negative). The same results are obtained with parthenogenetic activation of the egg.

We now find that exposure of unfertilized eggs to seawater containing NH_4OH at *p*H about 9 changes the properties of their membranes to those of fertilized eggs. In the terminology of our early work (see Fig. 1, curve *A*), the treatment induces the phase III events (the development of K^+-conductance and a potential of −60 mV) while bypassing the earlier events normally associated with the action of spermatozoa or parthenogenetic agents. The eggs remain unfertilized and can be fertilized later.

Unfertilized eggs of *Lytechinus pictus* were placed in normal seawater (*p*H 8.1–8.2) to which was added sufficient NH_4OH to bring the *p*H to 9.0–9.1, about 1 mmol of NH_4OH/l. An alternative method was to make the seawater 5–10 mM in NH_4Cl and to titrate it to *p*H 9.0–9.1 with NaOH. The methods for holding and penetrating the cells and for measuring potentials and resistances were those described earlier[1,2].

Fig. 1 shows the changes in potential in each case. After normal fertilization (Fig 1*A*) there is a phase I action potential, a phase II pause and a phase III development of the final potential of the fertilized egg. After exposure to NH_4OH seawater (*p*H 9.1) (Fig. 1*B*) the action potential is bypassed and the unfertilized egg enters and completes the phase III events. The effects of increasing the external K^+ concentration at the end of the experiment indicate that the potential is a K^+ concentration potential. After exposure to seawater brought to *p*H 9.1 with NaOH (Fig. 1*C*) the phase III events are induced, but only after a long time.

We interpret the development of the phase III potentials in the unfertilized egg in NH_4OH seawater as the consequence of an increase in the internal *p*H. The much slower development of potential in seawater containing NaOH is taken to mean that the NaOH penetrates, but much more slowly. These inferences are justified by a long standing permeability principle which states that weak bases penetrate in their undissociated form[4] and that the cell has little or no permeability to strong bases. The fact that the NH_4OH which penetrates increases the internal *p*H had been shown long ago in studies on sea urchin eggs, using *p*H indicators[5-7].

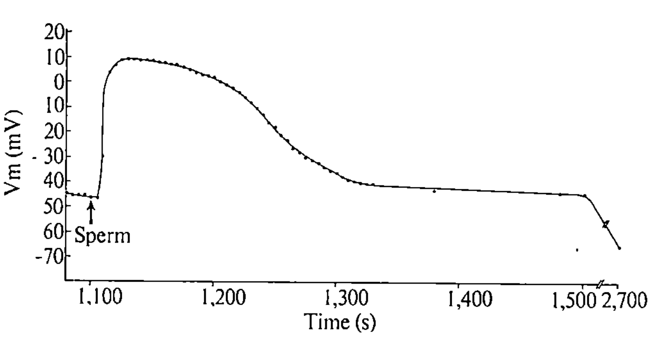

Fig. 2 Membrane potential changes upon insemination of an egg that had attained −45 mV after a 20 min exposure to NH_4OH seawater at *p*H 9.1. The depolarization and reversal of potential (action potential) indicate that the egg had remained unfertilized and capable of carrying out the phase I changes typical of normal fertilization.

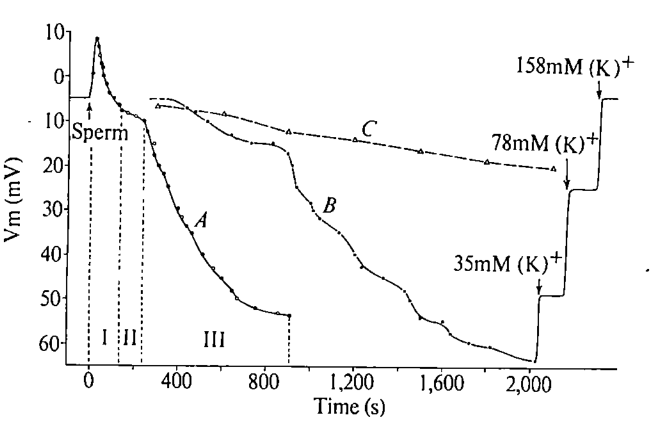

Fig. 1 *A*, Membrane potentials following normal fertilization. The phases I, II and III (ref. 1) are designated. *B*, Membrane potentials of an unfertilized egg exposed continuously to seawater adjusted to *p*H 9.1 with NH_4OH. After the potential had reached its final value, the external K^+ concentration was raised stepwise. The membrane potentials decreased as predicted for a K^+ concentration potential. *C*, Membrane potentials of an unfertilized egg exposed continuously to seawater adjusted to *p*H 9.1 with NaOH. Only the slow initial development is shown; the potentials ultimately reach −60 mV.

The effect of the NH_4OH in invoking the phase III development of membrane potential is not an "activation" of the egg in the sense in which that term is used by students of fertilization and parthenogenesis. As we have shown[1], parthenogenetic activation includes a phase I action potential; none is seen in experiments with NH_4OH. There is no cortical reaction in NH_4OH; no fertilization membrane is formed. (We note, however, Loeb's finding[8] that sea urchin eggs will develop if treatment with ammonia is followed by an exposure to hypertonic seawater.) After the membrane potential has developed in NH_4OH seawater, the egg may still be fertilized with sperm and then go through the cortical reactions, followed by mitosis and cleavage.

When sperm were added to eggs that had begun or completed the phase III reactions in HN_4OH seawater, fertilization was accompanied by a phase I action potential observed as a very large depolarization (Fig. 2). The eggs then repolarized, somewhat slowly, to the −60 mV typical of the end of phase III.

To test whether the NH_4OH seawater only initiated the phase III development of membrane potential or whether it was also required to sustain it, eggs were acidified after the potential had begun to develop. The medium was brought to *p*H 6.8–6.9 by addition of seawater containing butyric acid (final concentration about 2 mM). The development of membrane potential stopped (Fig. 3). In some experiments, potential was lost before it levelled off. Simultaneously the membrane resistance increased. After some time in acid conditions, the medium was again brought to *p*H 9–9.1 with NH_4OH. The membrane potential now increased very rapidly to the value it would have had if the egg had been in the NH_4OH seawater continuously. The rate of increase was far greater than would be expected if the return to alkaline *p*H had merely restarted the development of the potential at its normal rate. We interpret this sudden increase in potential as a "readout" of a latent K^+-conductance which had continued to develop in acid conditions.

We interpret these results as follows. (1) An increase in internal *p*H by NH_4OH initiates the development of K^+-conductance in alkaline conditions; this development is "read out" as increasing membrane potential and decreasing membrane conductance. (2) If the *p*H is lowered during phase III, the development of K^+-conductive sites in the membrane continues, but the channels are not open and the latent potential is not "read out". (3) With the return to alkaline conditions, the K^+-channels are opened and the potential is read out immediately. The same dependence of "readout" on *p*H is observed with normally fertilized eggs in phase III. In fact,

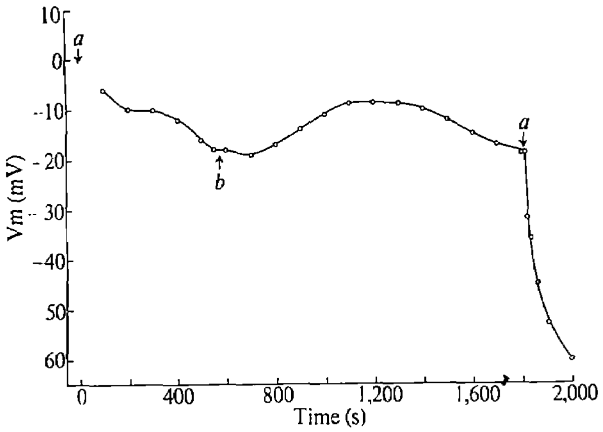

Fig. 3 Effect of pH on the development and "readout" of K^+-conductance. The development of potential is initiated in NH_4OH seawater. Neutralization of the medium with butyric acid to pH 6.8 arrests the development of measured potential, with a temporary loss of potential. Restoration of pH 9 with NH_4OH results in a rapid "readout" of potential, indicating the continued development of latent K^+-conductance during the period of exposure to acid. *a*, Basic seawater; *b*, acid seawater.

the progress of phase III in a fertilized egg is more rapid and more smooth in NH_4OH seawater than in normal seawater. So far we have not established whether or not the effect of pH on "readout" requires penetrating acids and bases.

In studies to be reported in detail elsewhere, we have asked whether the turning-on of the phase III membrane changes in the unfertilized egg by NH_4OH is accompanied by the release of other events that take place during the same period. From the time-table given by Epel *et al.*[9] the activation of the egg is followed immediately by cortical changes and respiratory changes during the first minute or so. The next sequence of events, beginning around the fifth minute, is the activation of some membrane transport processes, the initiation of DNA synthesis and the acceleration of protein synthesis. The latter group of events would coincide with phase III. We can report that the development of K^+-conductance in NH_4OH is accompanied by an increase of thymidine uptake, the initiation of DNA synthesis, the condensation of the chromosomes following DNA synthesis, and the breakdown of the nuclear membrane. No mitotic apparatus is formed. Protein synthesis is stimulated (experiments by D. Epel, in preparation). Thus, the presumed elevation of internal pH in an unfertilized egg that remains an unfertilized egg does release some important processes which normally follow after the activation of the egg by sperm.

We can imagine that among the first events of fertilization (for example, the respiratory burst and acid production) are some that change the intracellular pH, triggering the next group of events (the release of DNA and protein synthesis and the development of membrane properties). Our treatment with NH_4OH would be a replacement of mimicking of the normal link in the chain, starting those processes in an unfertilized egg that remains an unfertilized egg. The effect might be a common triggering of parallel events or might reflect a closer connexion between membrane potential and biosynthetic processes. Such connexions are being found in other systems[10]. The action of NH_4OH might in fact be an experimental substitute for a normal link in the chain, since it was reported long ago[11] that fertilization is accompanied by the production of ammonia.

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Influence of Sodium, Potassium and Chloride Ions on the Intracellular Responses of Turtle Photoreceptors

Vertebrate photoreceptors have a low membrane potential (about 30 mV) in darkness and respond to illumination with a hyperpolarization associated with an increase of membrane resistance[1].

The effects of ions have been studied in retinae of frog and pigeon by recording extracellular responses attributed to the receptors. In both cases the size of the response was linearly related to the log of external sodium ion concentration[2]. More recent work on the action of light on the sodium permeability of rod outer segments analysed in the isolated rat retina has shown that inward-directed current flows through the outer segment membrane in darkness and is reduced during illumination[3]. These observations suggest that vertebrate photoreceptors are highly permeable to sodium in darkness, and that light reduces sodium permeability and thereby increases the ratio of potassium to sodium permeability. If this interpretation is correct, membrane potential should be more sensitive to sodium concentration during darkness than during illumination and more sensitive to potassium concentration during illumination than in darkness. The experiments described here were performed to test these predictions.

The eye of the turtle, *Pseudemys scripta elegans*, was removed and cut along the medial-lateral axis. After draining the vitreous, the eyecup was mounted on a chamber where an oxygenated and buffered Ringer solution continuously flowed over the vitreous side of the retina at a rate of 5–6 ml./min. All solutions were freshly prepared: the pH was adjusted to 7.7 ± 0.1 with appropriate amounts of sodium bicarbonate or Tris chloride. Test solutions with low sodium concentration were made by replacing equimolar amounts of sodium chloride with choline chloride or Tris chloride or sucrose. Solutions containing potassium at high concentrations were prepared by replacing equivalent amounts of sodium chloride with potassium chloride. Solutions with low chloride concentration were prepared by replacing equimolar amounts of sodium chloride with sodium propionate or sodium sulphate. Intracellular recordings were made with glass microelectrodes, filled with 4 M potassium acetate. Responses were recorded differentially between two microelectrodes, one in the external solution and the other inside the cell. With microelectrodes of low tip potential[4] there was no need to correct the results for changes of liquid junction potentials due to substitution of the bathing fluids. The retina was stimulated by white light from a tungsten quartz-iodine lamp run from a regulated d.c. supply providing 6.5 A. The reduced image of a circular

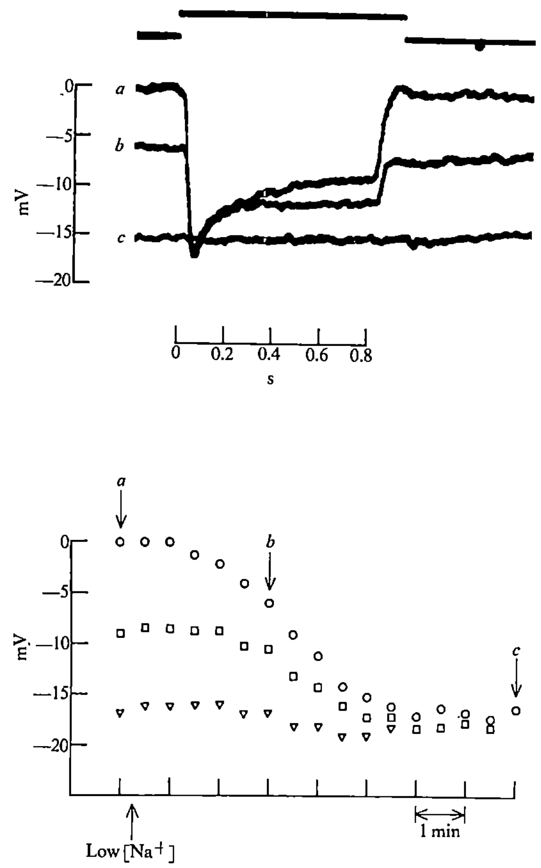

Fig. 1 Effects of low external sodium concentration on the intracellular responses of turtle cone. The records *a*, *b* and *c* on the top of the figure were taken at the times indicated respectively by the arrows *a*, *b* and *c* in the diagram below. At the time indicated by the upward directed arrow a sodium free solution made iso-osmolar with appropriate amounts of choline chloride starts substituting the control Ringer. The change of membrane potential is indicated relative to the transmembrane potential in darkness during the control period at the beginning of the experiment. The light intensity used to elicit the responses is 2.4 log units attenuated with respect to the total available energy. ○, Dark level; □, plateau of response; ▽, peak of response.

diaphragm was brought to focus on the retina where its diameter was 500 μm. The light intensity was attenuated by neutral density filters. The total irradiance of the unattenuated light of wavelength between 4,000 and 8,000 Angström was approximately 4.5×10^3 μW/cm^2.

The results of an experiment in which intracellular responses from a cone were recorded during perfusion of the retina with a sodium-free solution are shown in Fig. 1. The superimposed records (*a*), (*b*) and (*c*) at the top of the figure were taken at the times indicated by the arrows in the diagram at the bottom of the figure. In (*a*) light evokes the characteristic hyperpolarizing response in normal perfusing conditions; in (*b*) and (*c*) responses to light from the same cell were obtained at two different stages of sodium substitution. Clearly as the sodium-free solution exchanges with the normal Ringer, the membrane potential in darkness (circles) and the potential of the plateau of the response (squares) increase, while the potential at the peak of response is not appreciably altered. In all experiments the effects of low sodium concentration were reversed when the normal external concentration of sodium was restored.

The effect of high external potassium concentration was studied in separate experiments. A representative experiment is shown in Fig. 2. The records at the top were obtained in normal Ringer (*a*) and after exposure for several minutes to a solution containing 50 mM potassium (about twenty times the normal concentration) (*b*). The lower part of the figure is a plot of the membrane potential in darkness (circles), during the plateau (squares) and at the peak (triangles) of the response to light.

These results show that the membrane potential of turtle cones is controlled predominantly by the sodium concentration in darkness and by the potassium concentration at the peak of the response. This is consistent with the idea that in darkness the membrane potential is due to the shunting effect of a high sodium conductance.

The plateau of the light response is appreciably modified by changing the external sodium concentration. This could be due either to an increase of sodium permeability following the initial reduction produced by light, or to a more complex effect reflected on the cone response by the feedbaçk from the horizontal cells[5].

The external potassium concentration affects consistently the membrane potential also in darkness. This suggests that the ratio of potassium to sodium permeability is not negligible even in darkness.

The hyperpolarizing effect of light can then be explained by assuming that sodium permeability is decreased as a consequence of illumination and the membrane potential changes approaching the level determined by the electromotive force of the potassium concentration difference. It seems likely that the light-dependent sodium permeability is located in the membrane of the outer segments, and that the inner segments are constantly permeable to potassium[6].

I thank Drs M. G. F. Fuortes and E. F. MacNichol jun. for advice and criticism.

Note added in proof. While my manuscript was in the

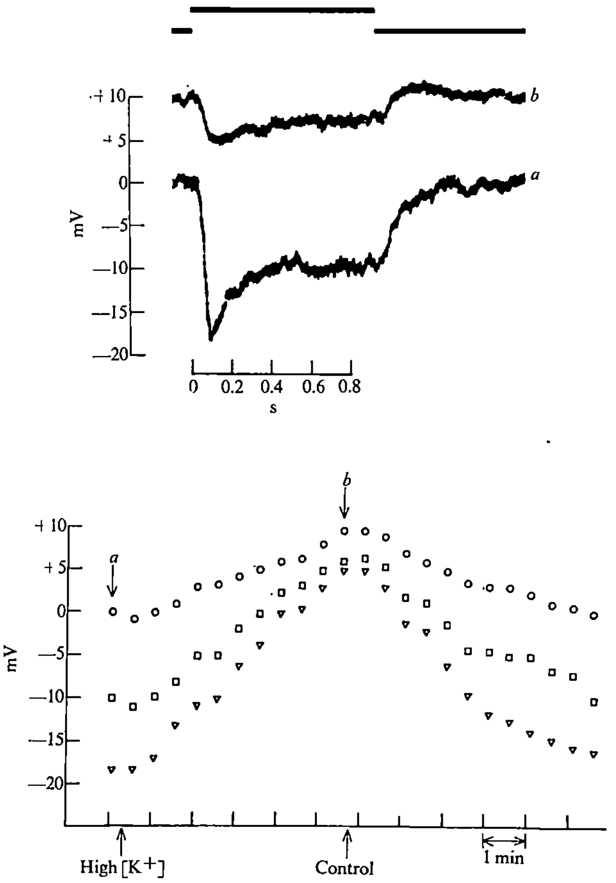

Fig. 2 Effects of high external potassium concentration on the intracellular responses of turtle cones. The records in *a* and *b* at the top of the figure were taken at the times indicated respectively by the arrows in *a* and *b* in the diagram below. The zero level of membrane potential indicates the level of membrane potential in darkness. At the time indicated by the upward directed arrow a solution containing 50 mM of potassium starts substituting the control Ringer. The stimuli parameters are the same as reported in the legend of Fig. 1. ○, Dark level; □, plateau of response; ▽, peak of response.

press, similar results on *Bufo marinus* retina have been obtained by L. H. Pinto and J. E. Brown: see the abstract in *Biol. Bull.*, p. 473, October 1972.

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Correlation of Cell Shape and Function in the Visual Cortex of the Cat

FROM recordings made with microelectrodes it is known that neurones in the primary visual cortex (area 17) of the cat's brain respond to certain types of visual stimuli. An individual cell usually responds well to slits or edges of light shone at an appropriate orientation within a particular part of the visual field. Such a cell can be classified as simple, complex, or hypercomplex, in terms of the selectivity of its responses[1,2]. Observations of Golgi-impregnated material have demonstrated that most cortical neurones are either stellate or pyramidal and it is natural to wonder whether the structural and functional properties of these cells are directly related. A suggestion that this may be so comes from the observation that the distribution of simple cells in different cortical layers tends to parallel the distribution of stellate cells, while a similar approximate correspondence exists between complex and pyramidal cells[1,3,4], which suggests this may be so. We have approached the problem of correlating cell structure and function more directly by injecting physiologically identified cells with a fluorescent dye, Procion yellow, using the technique developed by Stretton and Kravitz[5]. This dye spreads into even the finest processes of a cell and can give almost as clear a picture of cell morphology as a Golgi stain.

Cats were anaesthetized initially with ketamine hydrochloride, maintained in a state of light anaesthesia with intravenous thiopental sodium, and artificially respirated while paralysed with succinylcholine. A 2×5 mm region of the primary visual cortex was then exposed, coated with 2.5% agar, and covered with a transparent saline-filled chamber that was sealed to the skull. The sliding top plate of this closed chamber contained a small aperture filled with 'Vaseline', through which a microelectrode could be advanced into any desired part of the exposed cortex. Glass microelectrodes were prepared by bevelling the tips with a grinding stone[6] until the d.c. resistances were 20–80 MΩ and tip diameters 1–3 µm. The advantage of using bevelled electrodes is that their resistance is low enough to permit stable extracellular recording from cortical neurones, but they are sharp enough to penetrate cells.

In a typical electrode track through the cortex many single units were recorded extracellularly. The receptive field of each cell was mapped using spots and slits of light projected onto a tangent screen upon which the cat's eyes were focused. After the receptive field characteristics had been determined with the electrode positioned extracellularly, an attempt was made to penetrate the cell by advancing the electrode slightly. If a cell was impaled, its receptive field was quickly re-mapped to be absolutely sure that the intracellular and extracellular recordings were from the same unit. Occasionally an intracellular recording was obtained that was sufficiently stable to make it possible to map the receptive field even though the responses of the cell had not previously been recorded extracellularly.

When a cell was satisfactorily classified, it was injected with Procion yellow by passing a steady hyperpolarizing current of 1–20 nA for 1–30 min. The electrode was then withdrawn and a new penetration was made at least 0.5 mm from any of the previous electrode tracks. Up to a dozen separate penetrations could be made in an experiment, and each entry point of an electrode was indicated on an enlarged photograph of the surface of the cortex using the blood vessels as landmarks. At the end of the experiment an electrode filled with a [illegible] Chicago blue solution was used to make several superficial dye marks on the cortex. These served as reference points for identifying individual electrode tracks during histological processing. The animal was perfused with 10% formalin and serial frozen sections (80 µm thick) were cut from area 17 and examined with fluorescence microscopy[5].

In view of the numerous technical difficulties, it was not surprising that only one or, at most, a few cells were stained in each experiment. We have injected a total of sixteen physiologically identified neurones so far, and to illustrate our results we shall describe in detail two cells having particularly well-defined properties. The first of these cells responded optimally to a narrow slit of light moved slowly across its receptive field in a 2 : 00–8 : 00 orientation (Fig. 1A). This unit was clearly a simple cell, as defined by Hubel and Wiesel[1], because, on the basis of the responses to stationary spots and slits, its receptive field could be subdivided into a central "off" (inhibitory) zone flanked by antagonistic "on" (excitatory) regions. During subsequent histological examination of the cortex, a single fluorescent neurone was seen in the region where this unit was injected. The cell was located 350 µm below the pial surface, in layer IV a+b of Otsuka and Hassler[2] as determined from the cyto-architecture of an adjacent Nissl-stained section. A camera lucida drawing of this neurone shows a cell body about 15 µm in diameter and somewhat irregular in shape (Fig. 1*B*). Most of the processes radiating from the soma seem to be dendrites, because they divide into finer branches that are beaded and show occasional dendritic spines. One descending process, labelled "*a*", is more uniform in diameter, has no spines and is probably the axon. This neurone has the characteristic features of stellate cells seen in Golgi preparations of the visual cortex[3].

Fig. 2 illustrates a pyramidal cell injected in a separate experiment. The optimal stimulus for this unit was a vertical slit moved from right to left across its receptive field (Fig. 2A). Stationary vertical slits produced brisk discharges at "on" and "off" when positioned anywhere within the receptive field, but a rectangle filling the field gave only a weak response, indicating that this was not a simple cell. Nor was the cell hypercomplex, since the response to a slit was not diminished when the stimulus was lengthened so as to extend above and below the receptive field. It thus fulfilled the criteria for a complex unit. A partial photographic montage and a camera lucida reconstruction of this cell are shown in Fig. 2*B* and *C*. The pyramidal-shaped cell body is situated in layer V, 700 µm below the pial surface. A long apical dendrite radiates upward at least as far as layer III, and several basal dendrites and horizontal processes extend from the cell body. A descending process that is probably the axon can also be seen.

In some of the cells that were injected, either the functional or the morphological properties of the unit were not as clear-cut as in the two examples just described. For example, it was often difficult to map the receptive field of a unit, either because

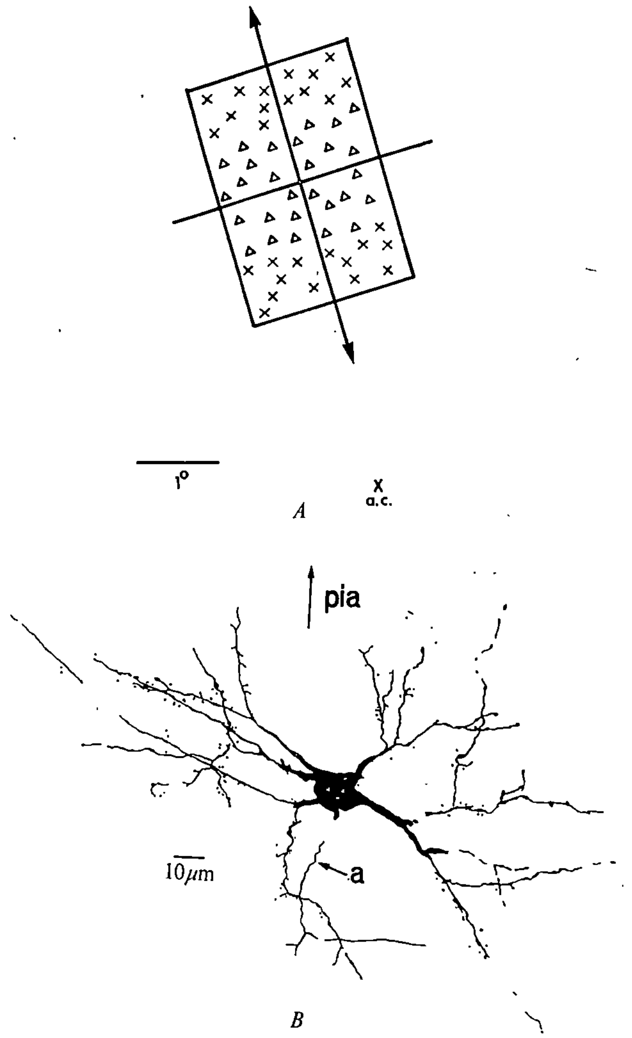

Fig. 1 *A*, Receptive field map of a simple cell that was subsequently injected with Procion yellow. This cell was driven by stimuli to the left eye; it responded best to a narrow slit of light held in a 2 : 00–8 : 00 orientation and moved in either direction orthogonal to the slit (arrows). Stationary spots and slits of light also drove this unit. X, Areas giving "on" responses; triangles, areas giving "off" responses. The cell showed only a 5 mV resting potential after penetration, but it was successfully stained by passing a steady 10 nA current for 20 min. The large X indicates the projection on the visual field of the area centralis (a.c.) of the left eye. *B*, Camera lucida drawing of the same cell, which lay in two adjacent coronal sections of the cortex. Drawings were made using bright-field fluorescence illumination and a ×100 oil immersion objective which allowed processes less than 1 µm in diameter to be visualized. Most of the branches emerging from the cell body show occasional faint appendages that are likely to be dendritic spines. One descending process "a" is more uniform and is probably the axon.

its responses were weak or because they were partially obscured by injury discharges produced by the electrode penetration. Further, the structural features of a neurone were sometimes intermediate between those of well defined stellate and pyramidal types, presumably because the cell was not completely stained. Many injected cells had to be discounted altogether for such reasons. Of the remaining sixteen neurones, nine were identified with a high degree of confidence, while the classification of the other seven was probable but not definite.

Most of the simple and complex cells that were injected conformed to a general pattern. Of the five clearly identified simple units, four were definitely stellate cells and the fifth was probably stellate also; one probable simple cell was definitely a pyramid. Five injected cells had well defined complex receptive fields; four of these cells were pyramidal and one was stellate. The three probable complex units were all pyramidal cells. We have also stained two hypercomplex cells, one of which was pyramidal and the other stellate. Both of these hypercomplex cells, as well as the two exceptions to the general pattern seen for simple and complex cells, were found in cortical layers II and III, suggesting that not only

Table 1 Summary of Identified Cells

		Definite	Probable
Simple cells:	stellate	4	1
	pyramidal	0	1
Complex cells:	stellate	1	0
	pyramidal	4	3
Hypercomplex cells:	stellate	1	0
	pyramidal	1	0

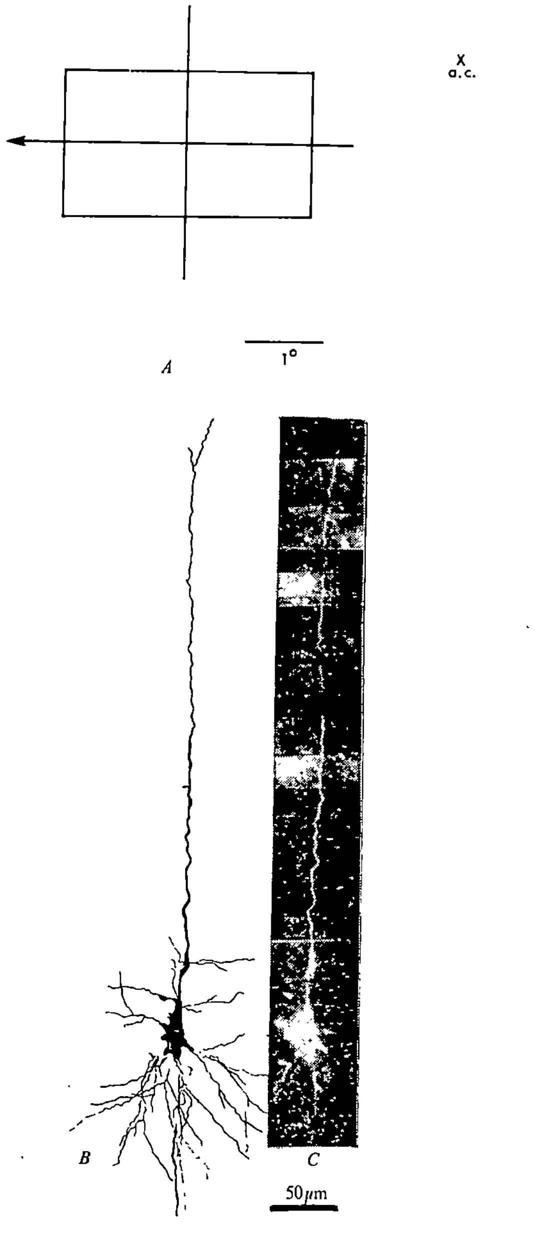

Fig. 2 *A*, Receptive field of a complex cell that responded optimally to a vertical slit. The cell was driven equally well by both eyes and had a moderate directional preference (right to left). Stationary vertical slits produced discharges at "on" and "off", but stimuli more than 30 degrees from vertical gave little or no response. The cell was penetrated without previous extracellular identification; the resting potential was 40 mV. To inject the cell, a 1–2 nA hyperpolarizing current was passed for 15 min. *B*, Camera lucida drawing of the same cell. The cell is similar in appearance to the large pyramidal cells seen in Golgi preparations. *C*, Partial photographic montage of this cell, which was a large pyramid situated in layer V.

cell shape but also location within the various layers of the cortex are functionally important.

These experiments demonstrate that it is possible to inject dye into individual stellate and pyramidal cells in the mammalian cortex. Although our electrodes may be biased towards selectively impaling relatively large cortical cells, we have been able to inject and recover neurones whose somata are less than 10 µm in diameter. Our results, while still preliminary, support the idea that the morphological and physiological properties of cortical neurones are closely related. Most injected simple cells were stellate, and most complex cells were pyramidal; we have not yet stained any of the cortical cells that are neither stellate nor pyramidal, such as fusiform or multiform cells. A larger sample of cells is obviously needed to determine more precisely the relationship between structure and function in each cortical layer. Our hope is that this approach will eventually lead to a more complete understanding of the different stages of information processing within the cortex.

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Thorne Moor: a Palaeo-ecological Study of a Bronze Age Site

A STUDY of the palaeo-ecology of an area in South Yorkshire has revealed an exotic element in the Bronze Age insect fauna (about 1100 BC), together with evidence for southerly restriction in the distribution of some British species. This fauna has been studied in relation to a number of archaeological features relating to forest clearance.

Thorne Moor (National Grid ref. SE 730160), a fast shrinking relict of a once extensive blanket bog, lies 15 km north-east of Doncaster. The area is largely below the 10 foot OD contour and is floored by lacustrine deposits of the last glaciation, which form a gently undulating topography originally covered by up to 2.0 m of peat (now largely removed for commercial exploitation).

In October 1971, Mr W. Bunting drew our attention to a number of large, superficially burned tree trunks being exposed by the cutting of drainage ditches. Subsequent investigation demonstrated two limited areas, one about 50 m across, wherein most of the large trees, which lie at the base of the peat, had charred surfaces. Much of the fossil timber, all from the lower 0.5 m of the peat, was riddled with insect galleries and a study both of this and of the associated organic muds and peat was initiated. During sampling, a number of parallel split timbers in a fresh ditch section were observed (J. R. A. Greig, personal communication). On excavation this was found to be part of a trackway of simple construction in the peat at the same level as many of the trees. This and the areas of burnt trees have been interpreted as representing a phase of small temporary clearances in the mixed oak forest, preceding the main period of peat formation on the Moor. The carbon-14 age of 3090±90 BP (Birm. 336) gives a Bronze Age date for these activities and agrees with the earliest clearance horizons defined on palynological grounds[1]. Dr M. Herbert-Smith has found significant quantities of cereal pollen between the timbers of the trackway. The insect fauna and plant macrofossils of this period indicate phases of open water, perhaps in the form of confluent pools, over much of the area, resulting in the decline and death of the forest trees. This process was sufficiently rapid for the deposits immediately above the forest soil, around the roots of trees which were still standing, to contain a mixture of many water beetles and insects associated with the moribund forest. The construction of the trackway was a response to the increasingly wet conditions, the waterlogging finally curtailing all agricultural activity in the area. Despite the complete absence of supporting archaeological data, the decrease in arboreal pollen during the Iron Age was interpreted as marking the onset of more intensive agricultural activity[1]; the end of the forest on Thorne Moor may now be ascribed to a cumulative and widespread process of flooding. The Moor lies well within the tidal reach of the Humber and, like the early post-Roman flooding at York[2], the mechanism may be changes in the configuration of the mouth of the Humber—the destruction by the sea of an earlier Spurn Point—increasing the access of the tides to the estuary, thereby backing up the outflow of the rivers and causing freshwater flooding.

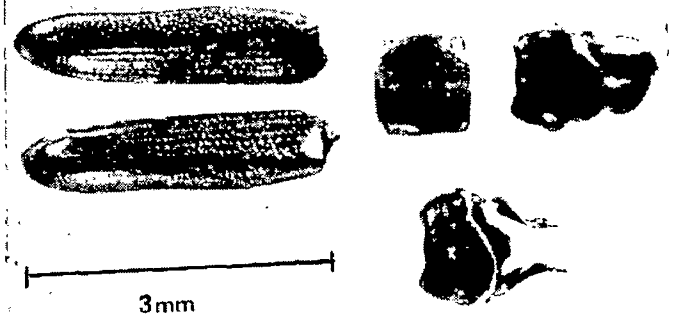

Fig. 1 *Prostomis mandibularis* (F).

The insect fauna includes non-British and Southern English beetles. Many well-preserved specimens of *Prostomis mandibularis* (F.) (Cucujidae) (Fig. 1) have been recovered, both from beneath bark and from associated organic silts, the greatest numbers coming from between the timbers of the trackway. All the examples from Thorne were associated with oak. The species, previously unknown in Britain, is recorded as living in the extreme south of Sweden, throughout Europe south of the Baltic, in the USSR and North America. It is regarded as a species of ancient forests and lives in wood which is in an advanced state of decay[3]. A single thorax of *Rhysodes sulcatus* F. (Rhysodidae) was found in an accumulation of silt in a hollow between the roots of a large oak stump. *R. sulcatus* now has a southerly distribution in Europe and is also known from the Caucasus and Anatolia[4]. It has been previously recorded from a deposit of Neolithic age (^{14}C age, 4830±100 (NPL 39)) at Shustoke in Warwickshire[5]. It is found in rotten wood and is probably a predator. *Zimioma grossa* (L.) (Ostomidae) (Fig. 2) has a wide boreo-montane distribution in continental Europe and across the USSR to Baikal. The larvae bore in rotten wood, pupation occurring in a dilation of the tunnel just beneath the bark. A single complete male individual was recovered from such a chamber below the bark of a birch, which lay in the upper part of the basal peat, probably dating from the Early Iron Age. It is worth noting that *Z. grossa* is recorded from old woodland which has been damaged by forest fires[3]. *Mycetina cruciata* Schall. (Endomychidae) shows a similar European distribution to *Z. grossa*[6]. It is locally common beneath the bark of both deciduous and coniferous trees, associated with Polyporus fungi. A single specimen was found between the wet, decayed timbers of the trackway. The Eucnemid, *Isorhipis melasoides*

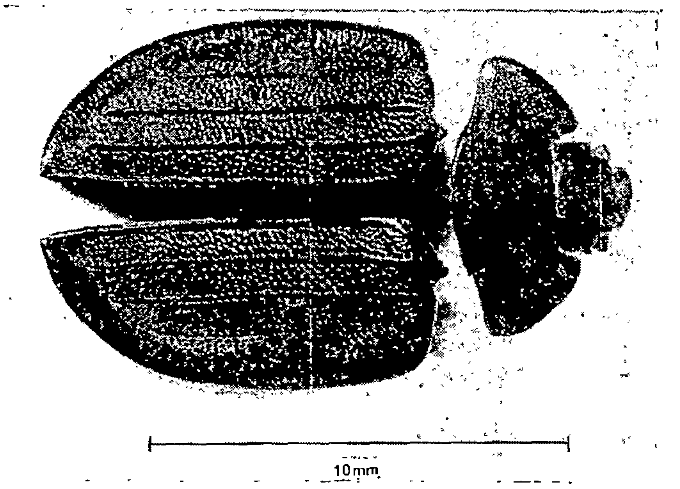

Fig. 2 *Zimioma grossa* (L.) ♂.

(Cast.), was at least occasionally abundant at Thorne; its characteristic workings were frequently noted and a number of complete adults and many larval head capsules were found by splitting timber. The species, normally associated with beech[7], is now rare on the Continent and is restricted to areas away from the western seaboard and the Mediterranean.

Further to this list from Thorne, it is relevant to include the specimen of *Cerambyx cerdo* L., found in a bog oak from the Cambridgeshire Fens[8]. This specimen has been re-examined and found to be contemporary with the wood, dated to 4000 ± 66 BP (Birm. 1). In agreement with Allen[9] and Morley[10], this species can now be finally removed from the list of insects which have lived in Britain since systematic recording began, probably having disappeared well before the advent of the early entomologists who erroneously recorded it.

A number of species found in the Thorne samples do not now live as far north as Yorkshire and have obviously restricted their ranges since the Late Bronze Age. These include *Colydium elongatum* (F.), *Dryophthorus corticalis* (Payk.), *Hypulus quercinus* (Quens.), *Mesosa nebulosa* (F.), *Micromalus parallelopipedus* (Hbst.), and *Platypus cylindricus* (F.). All are associated with wood. In addition, Skidmore has recorded *Gnorimus nobilis* (L.) from a deposit of similar age at Askern, 10 km north of Doncaster, well north of its present distribution[11].

The disappearance from Britain of the five species from Thorne, of *C. cerdo*, and of the dung beetle *Aphodius quadriguttatus* (Hbst.) and *Dermestes laniarius* Ill., a relative of the common bacon beetles, recorded in the fauna from the Wilsford Shaft, Wiltshire (3330 ± 90 BP (NPL 74))[12], and the restriction in range of many others depends on a number of factors. The hypothesis of climatic changes towards a more oceanic regime is supported by the present European distributions of these species, which in general exclude areas of damp mild climate. This correlation may not, however, be justified for, as Osborne has suggested[13], the anthropogenic factor must always be considered once man has started to break the forest cover. The Thorne fauna is contemporary with such an event and, although the total disappearance of dense woodland in this locality is related to geomorphological factors, elsewhere it is evident that, as clearance proceeded, habitats became both restricted and separated. Many species dependent on mature forest must have been reduced to populations whose small size would render them liable to extinction by any minor environmental change, the isolation of each community precluding re-immigration. The German word *Urwaldtiere*—old forest animals—would seem most appropriate for such insects[14]. A good example is provided by *Teredus cylindricus* (Ol.) (Colydiidae). The beetle, abundant in the Thorne trackway samples, is now rare, restricted to parts of Sherwood Forest and Windsor Forest, poor substitutes for the ancient forest environment. This species and many others associated with rotten wood habitats must be regarded as endangered animals, not only in Britain but throughout Europe.

This note owes much to the work and stimulating discussion of P. J. Osborne and to W. Bunting's untiring efforts to protect what is left of Thorne Moor. Professor F. W. Shotton kindly read and commented upon the manuscript. This work was carried out during the tenure of NERC grants.

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Ultraviolet Differences between the Sulphur Butterflies, *Colias eurytheme* and *C. philodice*, and a Possible Isolating Mechanism

Two common North American "sulphur" butterflies, *Colias eurytheme* and *C. philodice*, hybridize widely over much of the United States. The planting of dense agricultural stands of larval foodplants, together with habitat destruction starting about 1850, are believed to have affected the species' geographical ranges and abundances, causing extensive sympatry over much of the eastern United States[1], setting the stage for introgression. Taxonomists have tried to separate the species on the basis of visible wing coloration, but this varies continuously from orange (pure *eurytheme*) through yellow–orange (*eurytheme* and many hybrids) to yellow (*philodice* and rarely *eurytheme*). Female polymorphism and numerous described infraspecific taxa compound the taxonomic confusion. Although some of this variation has been attributed to genetic (refs. 2 (and references therein) and 3) and environmental factors[4], species determinations are often guesswork. We wish to point out two correlated qualitative characters that can be used to separate these species. One character, ultraviolet reflexion, may be more than a taxonomic tool—it may be the butterflies' own *carte de visite*.

Males of *eurytheme* have a brilliant ultraviolet reflexion pattern (Fig. 1), easily visualized by ultraviolet video-viewing[5] or photography. The iridescent coloration, of structural origin, is produced by interference in layered lamellae that make up the ribs of special wing scales (R. Silberglied, thesis, Cornell University, 1969; Figs. 2*b* and 3*b* of ref. 6 vaguely show the lamellar structure, although the authors do not comment on it). Superficially identical structures occur in wing scales of *Eurema lisa* (Pieridae)[7]. These scales, and the ultraviolet pattern they produce, are absent in males of *philodice* and in all females of both species. Although the lamellar structure of the ribs cannot be resolved with the light microscope, visible correlates can. The distance between the parallel ribs of ultraviolet-reflecting scales is considerably less than that of other scale types (Fig. 2). Their lack of distal lobing[8,9] is often distinctive. The ultraviolet reflexion pattern of male *eurytheme* usually corresponds with the distribution of visible yellow or orange coloration, but the veins, which lack these scales, are dark. Correlation of scale structure with ultraviolet reflexion has also been reported in *Gonepteryx* (refs. 10–16 and those in ref. 12), and *Pieris*[17].

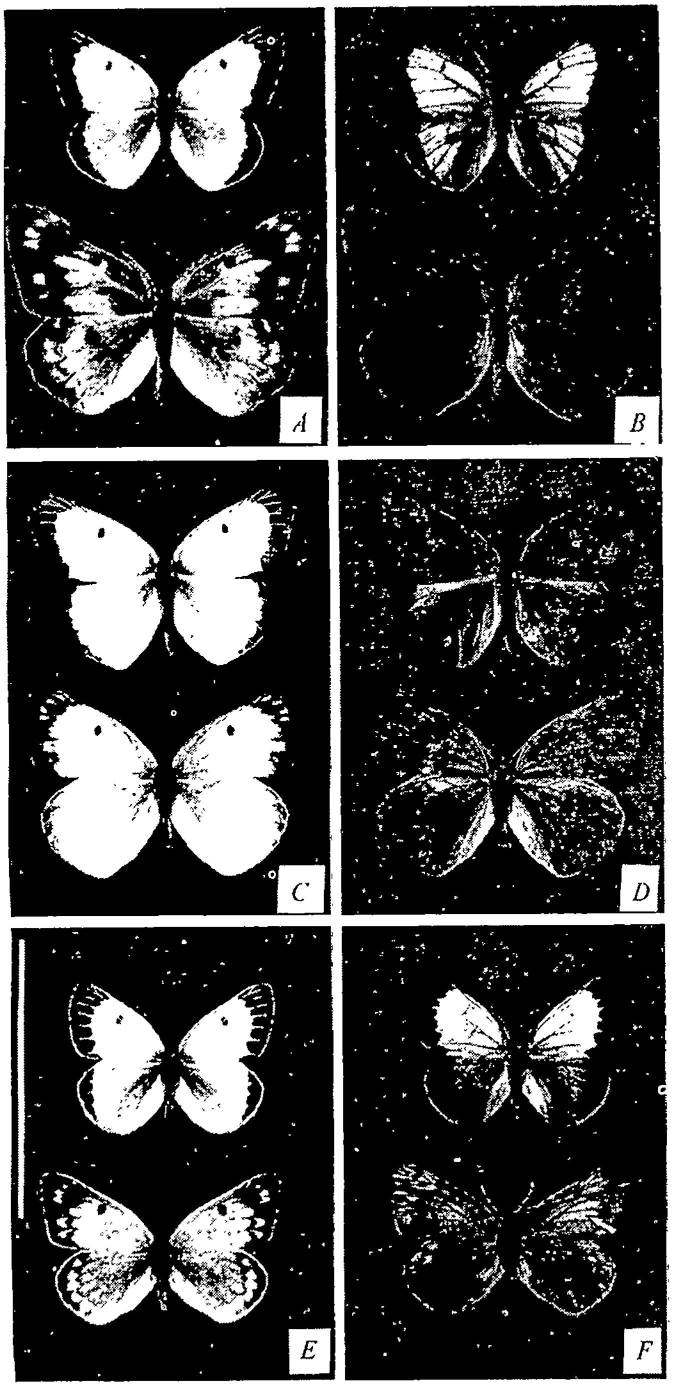

Fig. 1 *Colias eurytheme* (visible coloration orange; *A*, *B*), *C. philodice* (yellow; *C*, *D*), and *C. chrysotheme* (orange; *E*, *F*) in visible (400–700 nm, left) and near ultraviolet (300–400 nm, right) light. The male is uppermost in each photograph. Arrow in *F* indicates UV-reflecting patch of female *C. chrysotheme*. Reference line for all figures (in *E*), 5 cm. (*A*, *B*: male, Elsinore Lake, California; September 1, 1917; female, Columbus, Georgia, July 23, 1944; *C*, *D*: male, West Newton, Massachusetts, September 6, 1900; female, Tyngsboro, Massachusetts, July 22, 1914; *E*, *F*: male, Leitha Gebirge Mountains, Austria, 1928; female, vicinity of Vienna, Austria, 1936.)

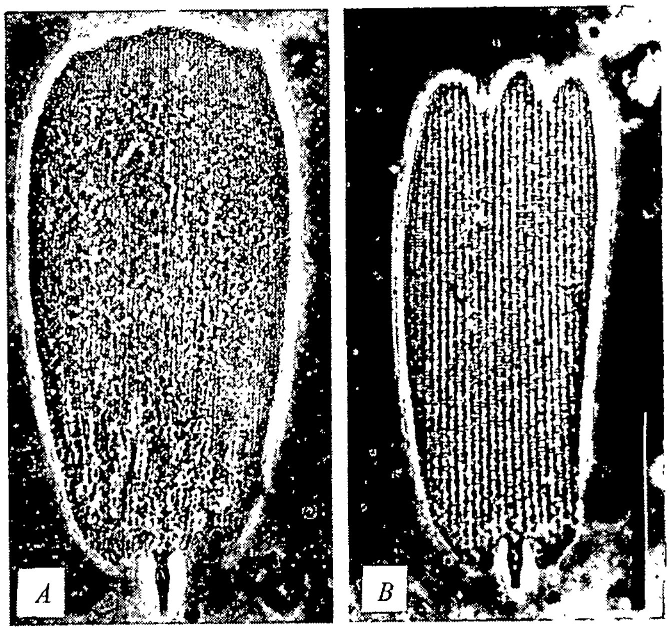

Fig. 2 Uppermost ("cover") wing scale of male *Colias eurytheme* (*A*), characterized by ribs about or less than 1 μm apart, reflects ultraviolet light; that of *C. philodice* (*B*), with a wider rib spacing, does not. Apical lobing of the scale may not be diagnostic for lack of reflexion. The lamellar structure of the ribs (in *A*), responsible for ultraviolet reflexion, cannot be resolved with the light microscope. Reference line for both figures (in *B*), 50 microns; polarized phase illumination.

Ultraviolet reflexion is a qualitative character. Examination of natural and laboratory-reared males of both species and interspecific hybrids has revealed only two phenotypes: ultraviolet-reflecting and ultraviolet-absorbing. This contrasts with the highly variable, pigment-produced, visible colours of *Colias*.

More than 12,000 male specimens, representing all described geographical units of *eurytheme* and *philodice*, were examined. All (>1,000) male specimens from allopatric *eurytheme* populations are ultraviolet-reflecting, including seven *yellow* specimens from the southern United States and Mexico. All (>500) allopatric male *philodice* (including "eriphyle" and "kootenai") are ultraviolet-absorbing. (Males from the isolated Guatemalan population of "*philodice*" are ultraviolet-reflecting but have a pattern different from *eurytheme*, and represent a population of a different species complex.) Most field-collected yellow–orange specimens from areas of sympatry, suspected of having an F_1 or other hybrid origin, are ultraviolet-absorbing, but a small proportion are ultraviolet-reflecting. All (>10,000) females examined are ultraviolet-absorbing. White ("alba") females reflect slightly more than "normal" females, but are never iridescent. Specimens of *eurytheme* collected early or late in the flight season, charac-

Table 1 Ultraviolet Phenotypes of Gerould's[18] Two Largest F_2 Interspecific Crosses, Demonstrating Sex-linked Inheritance of Ultraviolet Reflexion in *C. eurytheme* and *C. philodice*

Gerould's cross number	1913q	1914g
P_1♂	*Philodice*	*Eurytheme*
P_1♀	*Eurytheme*	*Philodice*
Expected F_2 ratios (males)		
If sex-limited only	3 UV− : 1 UV+	3 UV− : 1 UV+
If sex-linked	All UV−	1 UV− : 1 UV+
Observed (males)	13 UV−	8 UV− : 7 UV+

UV−, ultraviolet-absorbing; UV+, ultraviolet-reflecting.

terized by a localization of orange colour, have the same ultraviolet reflexion patterns as those collected in midsummer. Even the rare all-black males have the characteristic ultraviolet reflexion patterns.

All 155 F_1 male progeny of thirty-two interspecific crosses, involving both male *eurytheme* × female *philodice*, and male *philodice* × female *eurytheme*, were ultraviolet-absorbing. Examination of Gerould's classic F_2 broods[18] at Yale University[19] (Table 1), as well as numerous recent experimental crosses (by O. R. Taylor), revealed that the ultraviolet-reflecting character is inherited as a sex-linked recessive. The genetics of interspecific ultraviolet pattern inheritance will be treated in detail elsewhere (R. E. S., O. R. T. and S. A. Ae, in preparation).

Allopatric populations of *eurytheme* are homozygous for the (ultraviolet-reflecting) recessive allele (*uu*) and allopatric *philodice* populations are homozygous for the (ultraviolet-absorbing) dominant allele (*UU*). Sympatric populations in Arizona where interspecific mating is frequent, as well as laboratory crosses, contain yellow (*philodice*-like) but ultraviolet-reflecting, and orange (*eurytheme*-like) but ultraviolet-absorbing individuals, indicating that the ultraviolet alleles segregate from colour alleles and introgress into both parental populations.

Interspecific mating between these two species is not random[20], as had been reported[21,22]. In the American mid-west and Arizona, comparisons of mating pair samples ($N = 6,032$) from sympatric populations with random samples of adults show that mating is always positively assortative and differs significantly from random. Interspecific mating increases with density. The explanation lies with female behaviour during maturation. Mating obtained in the field with females of varying ages has shown that interspecific mating occurs almost exclusively when males can find and mate with freshly-emerged females (<1 h old) that are too young to reject them—a common phenomenon in dense populations in Arizona. Female mating preferences were determined by: (1) observing the courtships and matings ($N > 3,000$) of 100–150 virgin females of each phenotype in mixed populations; (2) comparing the expected and observed frequencies of the different mating combinations in large samples of field-collected mating pairs; and (3) obtaining matings in a mixed population in a large outdoor cage (O. R. T., thesis, University of Connecticut, 1970).

Virgin females of *eurytheme* reject the courtship attempts of F_1 hybrid, ultraviolet-absorbing (*Uu*) males, while females of *philodice*, whose natural mates are also ultraviolet-absorbing, accept them (O. R. T., in preparation). Sampling from an area of recent sympatry in Arizona shows that males possessing unusual colour and ultraviolet combinations are at a disadvantage in mating. Selection seems to act against ultraviolet-reflecting hybrids (that is, F_2, or $F_1 \times$ *eurytheme*) through the mate-selecting preferences of the females. In an Arizona population significantly fewer ultraviolet-reflecting hybrid males were found among mating pairs (1.2%/662) than expected based on the frequency of these males in random samples (5.7%/653; $\chi^2 = 25.14$, $P < 0.001$). Such evidence supports the hypothesis that the ultraviolet character functions as an isolating mechanism, or is highly correlated with an isolating mechanism that is unspecified at present. The ultraviolet character, however, is not the only isolating mechanism involved, since one of us[23] has shown that olfaction plays a major role in mate-selection by females. The latter result suggests that pheromones produced by the male are also used during courtship.

Visual stimuli release courtship behaviour in most butterflies, including *Colias*. Sexual dimorphism of ultraviolet reflexion is common throughout most of the Pieridae[10–12] and those species tested behaviourally[24–26] and electrophysiologically[27] (*C. eurytheme*) are sensitive to ultraviolet light. In Japanese *Pieris rapae*, ultraviolet reflexion of female wings releases male courtship behaviour[25]. *C. eurytheme* males approach females much more frequently than they approach other males, indicating that males may use the ultraviolet pattern to distinguish between the sexes. These facts, together with evidence that mating behaviour in pierid butterflies is affected by light intensity and spectral quality[25], suggest that ultraviolet patterns function in mate-selection in these species.

Finally, our species of *Colias* are not synonymous with the palaearctic *C. chrysotheme*, as some previous authorities have contended[28,29]. Unlike both *eurytheme* and *philodice*, both sexes of *chrysotheme* have iridescent ultraviolet reflexion (Fig. 1). Other problematic species and species groups in the genus can be readily characterized by means of ultraviolet reflexion patterns (R. E. S., in preparation). It has been stated that *Colias* could not be monographed because of “variation and hybridization problems[30]”, and that “no other genus of butterflies . . . presents so many baffling and stimulating problems[31]”. Some of the answers, it now seems, have been elusive simply because they lie beyond our visible spectrum.

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BOOK REVIEWS

Violence in Perspective

The Challenge of Violence. Edited by Derek Richter. Pp. 174. (Ardua: Tadworth, Surrey, 1972.) £1.90.

Is Peace Inevitable? Aggression, Evolution and Human Destiny. By Santiago Genovés. Pp. 194. (George Allen and Unwin: London, August 1972.) £2.50.

It is seldom that a brace of books arrives on one's desk of which, having read, one can speak with unrestrained enthusiasm. Both deal with violence and hostility in the world of man, and each makes a genuine contribution toward the clarification of the issues, and at the same time offers realistically practical suggestions directed toward the solution of these problems.

The Challenge of Violence is published under the auspices of Amnesty International, which will receive proceeds from the sale of the book. Let me say at once that I have never read a volume by different contributors in which each of their essays is of such sterling quality, and which together so beautifully intercorrelate and reinforce one another. Usually such volumes are something less than exciting. This one I read, as Shelley used to say, in a frenzy of enthusiasm. *The Challenge of Violence* is the best symposium of its kind I have ever read. Dr Derek Richter's introductory essay, "Psychiatric Aspects of Violence", is certainly one of the best balanced analyses of the nature of violence with which I am familiar. Dr Richter sees violence as a form of insanity, and faulty upbringing at the heart of the problem. Education in the ability to think and to feel as an interdependent humane being, principally achieved through reconstituted schools, is impressively discussed by Geraldine Lack in "The Contribution of the Schools". Alan Bestic examines the prevailing violence in Northern Ireland, in an essay curiously mistitled "Inter-Racial Violence". But it is nonetheless illuminating, for all that. William Burrows, psychiatrist, writes with wisdom and insight on "Students in Revolt" on American college campuses, and David MacSweeney helpfully discusses "The Concept of Maturity", a stimulating analysis for a world in which too many people grow older without growing up. But should one really ever grow up? MacSweeney himself speaks of Bertrand Russell, "the most brilliant child who ever lived to be nearly a hundred". Paedomorphosis is a very good idea. In "Women Working For Peace" Frances Eliot rightly emphasizes the importance of working within an organization, and in a moving essay, "Prisoners of Conscience", Eric Baker shows how successful organizational efforts can be in the rescue of political prisoners from governments who often do not know how large their number is. Is it not time that the unquestionable authority of the state were questioned? And what is the state if not an abstraction consisting of men? And is it not men, rather than abstract entities called states, who commit crimes against humanity? And should they not be held responsible for their crimes against humanity, such men? And was not that the principal injunction of the Nuremberg Tribunal?

In "The International Arms Race" Robin Clarke offers a thoroughgoing anatomy of the contribution of scientists and technologists to the progress of nuclear suicide, and the somehow inviolable notion that science must go on. "If such high proportions of our science and technology are used for military ends, it would obviously be a safer world if there were less science and technology." Finally, Sir Geoffrey Vickers in "The Containment of Conflict" gives us a really brilliant exposition of the conditions necessary for the achievement of a stable peace between modern societies. It forms a quite admirable pendant to this jewel of a book.

The Challenge of Violence is a book which should be read by everyone who considers this world worth saving. I hope the book is read in schools and universities. It would make a fine whetstone upon which to sharpen one's wits in study groups, seminars, and in similar discussion groups.

Is Peace Inevitable? by the Mexican anthropologist Santiago Genovés, is subtitled "Aggression, Evolution, and Human Destiny". It is a splendidly sound and clarifying volume. Genovés is one of those physical anthropologists who fully understands that a knowledge of man's social evolution constitutes an indispensable dimension of the physical anthropologist's equipment. He writes with impressive authority from the holistic viewpoint of man's biosocial evolution. What Genovés is principally concerned with is the critical examination of current popular theories concerning man's nature and the nature of war. The theories of Lorenz and Ardrey come in for particular treatment, and are disposed of in masterly fashion. The fuzzy concept of "aggression" is carefully dissected, and the nature of aggression among animals clearly explained. In *On The Origin of Species By Means of Natural Selection, Or The Preservation of Favoured Races in the Struggle For Life* (the full and significant title is seldom given), Darwin, in using the phrase "the warfare of nature", confirmed and perpetuated the prevalent view. The idea more than lingers on. Some day, when the social history of biological thought comes to be written, future readers will be astonished to learn how much of biological theory was influenced by sociopolitical thought.

It is not an accident that the rise and popularity of the Lorenz–Ardrey interpretations of man's "aggressive nature" should be so appealing in this age of violence. The new social Darwinism is paying high dividends because, among other things, it is so consoling to know that violence is "in the nature of things", and especially in the nature of man. The burden of guilt is relieved, and one may in good conscience acquiesce in every form of sanctioned violence with the sort of rationalized disengagement that contributes so massively to the perpetuation of state violence and the increase of individual violence. It is the state of mind of the majority of Americans who believe that what their government has been doing in Vietnam is in the interest of peace. Violence, of course, is not violence when it is used to repel violence. And so the debasement of thought and language goes on, and *Nineteen Eighty Four* is well on its way.

It is good to have such a book as Dr Genovés's at this time, for while he is a master at correcting epidemic errors, he is also full of hope. With the authors of *The Challenge of Violence* he independently looks for our salvation in the direction of education for humanity, in the necessity of love. *Is Peace Inevitable?* is a book of outstanding merit.

ASHLEY MONTAGU

Scanning Monographs

The Scanning Electron Microscope. By C. W. Oatley. Part 1. *The Instrument.* Pp. viii+194. (Cambridge University: London, September 1972.) £5.30; $16.50.

The Use of the Scanning Electron Microscope. By J. W. S. Hearle, J. T. Sparrow and P. M. Cross. Pp. xi+278. (Pergamon: Oxford and New York, September 1972.) £8.80.

THE scanning electron microscope is outstanding among modern scientific instruments, a type case in the techno-economics of innovation and at the same time spectacular in its results. In the form now generally available, and used for the study of surfaces, it is of entirely academic provenance, having been devised and developed in the Engineering Department of the University of Cambridge under the guidance of the author of one of these books, C. W. Oatley. To an even greater extent than the conventional transmission electron microscope, which came out of the Technische Hochschule of Berlin, the scanning microscope was born by technological expertise out of scientific curiosity. Ten years in gestation and upbringing, it was gradually refined in efficiency of operation and tested on such applications as were ready to hand. Only then was it adopted by an instrument making firm next door, and fully developed as a research tool. Its success in the market has been remarkable as the value of scanning microscopy for surface investigation came to be appreciated. Because the displayed image is responsive to the electrical, magnetic and in some degree also the chemical state of a surface, as well as to its topography, the instrument has found application in almost all branches of science and technology, in biological as well as metallurgical, solid state and polymer laboratories. A variety of models are now available, made by several small firms in addition to the main manufacturers of electron microscopes (the appendix in Hearle, Sparrow and Cross's book lists twelve makers).

For such a widely used instrument it is surprising that there has not been until now an authoritative handbook. We have had survey articles and conference proceedings a-plenty, but no comprehensive treatment of the subject. At last the situation is on the way to being remedied. Oatley himself has written the first part of a monograph, dealing with the instrument itself, to be followed by an account of its applications and of some related instruments. With a simultaneity not unusual in scientific publication, a team of practitioners of the art now offer a more practical text on the operation and applications of the scanning microscope.

To some extent the two books cover the same ground: in respect of the design and operation of the instrument, and the interaction of electrons with a solid sample. Not unnaturally Oatley's treatment of these topics is much the more detailed. He gives, for example, thirty-four pages to the electron gun as against two in the other text, and twenty-six pages (two) on signal collection and amplification. The two treatments of electron interaction with solids have much more in common, especially on secondary emission, which is basic to so many applications. Surprisingly, Hearle *et al.* have little to say about back-scattering phenomena, but on the other hand they include the Auger electron and cathodoluminescence modes of image formation, not mentioned by Oatley. In all other respects the two books cover entirely different ground.

The chief emphasis in Oatley's monograph is on the physical principles and technical features of the instrument. The fundamental limitations on the design of a scanning microscope are thoroughly discussed in chapter 2, the component parts of it in the next chapter, and electron interactions in chapter 4. The final chapter considers the various mechanisms contributing to image contrast, and then the factors that determine image resolution when examining solid surfaces. The scanning transmission microscope is to be treated in part 2.

In the meantime Hearle, Sparrow and Cross have provided an excellent survey of the subject as a whole which, if short on its fundamental science and engineering, is long on its multifarious uses. After the opening chapters, there follow accounts of specimen preparation and instrument operation, and then of applications in metallurgy, fibres and polymers, solid-state electronics and biology. The remaining chapters deal with fault-finding, dimensional measurements (including stereography), management of a scanning microscopy unit (including how to cope with visitors) and the future of the subject. To cover such a wide field would be expecting too much of a single author. The three named on the book's title-page have found it desirable to call in other specialists, and in fact the team of contributors numbers eight in all.

Their book is readable and well printed, illustrated with a wealth of micrographs, many of the high photogenic quality for which scanning electron microscopy is renowned. There are bibliographies after each chapter and a useful list of manufacturers and suppliers at the end of the text. It will rank as the standard handbook for users of the instrument (the authors state there were more than 500 of them in 1970), at least until part 2 of the Cambridge monograph appears. Part 1 provides the requisite background of the physical principles, engineering design and parameters of performance of the microscope itself. Oatley's treatment is elegant, concise and up-to-date. It is not often that the progenitor of a new research technique of such importance spares the time and has the ability to write the definitive account of it.

V. E. COSSLETT

Weatherwise?

Weather Forecasting for Agriculture and Industry. Edited by J. A. Taylor. Pp. xix+250. (David and Charles: Newton Abbot, November 1972.) £5.75.

A RECENT symposium associated with the University College of Wales at Aberystwyth took as its subject the forecasting of weather for social and economic needs. The contributions have been collected into this attractive book of seventeen chapters, complete with diagrams, a selected classified bibliography and indexes.

The principal theme is weather forecasting from both the sending and the receiving ends, with the suggestion that improvements in the quality of the predictions must be matched with the more frequent and more intelligent and wider use of them. There are, this text makes clear, meteorological forecasts for all sorts of users but the main classes of beneficiary are farmers, industrialists, hydrologists and tourists. Apparently the meteorological services must aim at supplying more short- and longer-term predictions accurate enough, if fully and intelligently applied, to lessen the costs or raise the profits of economic concerns and reduce the risk of inconvenience to a comfort-demanding society.

Here the problem is discussed by twenty practitioners expert in at least one of the weather-sensitive activities. Not surprisingly, the cumulative result is attractive and authoritative. Longer-range forecasting will prove increasingly beneficial to research, management and decision-making in agriculture, to constructional engineering, and to the development of tourism. Other cognate themes incorporate weather influences in the prediction of the demand for electricity, in the vagaries of river flow, and in the effect upon local climates of the extension of built-up areas. The many specific topics covered are exemplified by the discussions on the influence of weather upon the following: the daily attendance at recreational districts; the optimum amount of salt to prevent icing on roads; the growing of early potatoes; and fluctuations in the demand for beer.

Throughout the book the exposition and diagrams are lucid and effective, and the approach is highly practical and orientated toward cost-benefit and minimum-risk analysis. Most readers will quickly be convinced that in an intensifying economy with soaring prices of labour, goods and services, more attention should be given to applied meteorology in order to extract the maximum benefits and to ensure the minimum losses and waste in all weather-sensitive occupations. Undoubtedly the message set out here will attract and be easily intelligible to a wide range of persons, practical and academic. But it is to be hoped that an eleemosynary edition will be issued to bring the volume within the purchasing power of undergraduates who will also find the contents much to their liking. Then perhaps in their day they may convert the British from being a nation of indecisionists in weather affairs into a society that treats the financial and social aspects of climate with due respect and sanity.

ROBERT P. BECKINSALE

Molecular Structure

Molecular Geometry. By R. J. Gillespie. Pp. ix+228. (Van. Nostrand Reinhold: London and New York, July 1972.) £4 cloth; £2 paperback.

The Electronic Structure of Organic Molecules. By T. E. Peacock. (*The International Encyclopaedia of Physical Chemistry and Chemical Physics.* Vol. 2. Topic 4. *Electronic Structure of Molecules.*) Pp. xi+145. (Pergamon: Oxford and New York, July 1972.) £3.50.

IN the first of these two books Professor Gillespie has written the first full-length account of the valence-shell electron-pair repulsion theory of molecular geometry. The original introduction of the theory goes back to Sidgwick and Powell in 1940, but the greater part of its subsequent development is due to Nyholm and Gillespie himself. The basic idea is simple; it is that, except for very polar (near-ionic) systems, molecular shape is determined by the very large repulsions which exist between lone pair electrons and the smaller repulsions between electrons involved in bonding in the valence shell of a central atom. No precise description of the detailed shape or character of these electronic orbitals is attempted: and indeed Gillespie sometimes speaks of an orbital as a part of a space or a region, and sometimes as an electron cloud.

After a few introductory chapters in which the basic ideas are expounded, most of this book is devoted to understanding particular geometries in the light of the fundamental rules. It is quite astonishing to see how successful the method is, even though adherents of the more traditional theories may be a bit horrified to be told that there may be up to eight distinct valence-shell orbitals. This part of the book is admirably illustrated, with a wealth of information not readily available elsewhere.

There are strengths and weaknesses in this theory. Its strength is that so much experimental information is so nicely rationalized. Its weakness is that it is not susceptible to any numerical application, and that it disregards so much that is well known about orbitals in atoms. Moreover, without considerable extension, it cannot tell us much about the shapes of molecules in excited electronic states. Its failure to take account of our knowledge of atomic orbitals explains why the theory cannot naturally explain such matters as the difference between the linear structure of $HgCl_2$ and the angular structure of $BaCl_2$ or the charge distribution in N_3^-, whereas simple considerations of hybridization do so. The book would have been much strengthened if a more effective link could have been provided between the new and the old theories.

Read in conjunction with traditional texts and particularly as regards the qualitative insights that it provides, this can be a very useful book.

Dr Peacock's book is of a different kind. His concern is with the traditional theory of π electrons; moreover the first two-thirds of the book is devoted to the Hückel theory, and only the last forty-four pages deal with improved theories. The material covered is similar to that in many previous texts; presumably this book was written because it was felt that the complete series needed something of this form. The volume has a rather old-fashioned character. The author is more at home with the calculation of energies than of other properties, and he provides some useful tables for comparison between theory and experiment. Unfortunately the proof-reading is atrocious, and there are rather more distinct errors than one would have wanted in a volume intended for student use.

C. A. COULSON

Pertinent Biology

The Future of Man. Edited by F. J. Ebling and G. W. Heath. (Proceedings of a Symposium held at the Royal Geographical Society, London, on April 1, 1971.) Pp. xviii+211. (Academic: New York and London, February 1972.) £2.80; \$8.95.

THE symposia of the Institute of Biology are now an established event in the biologist's calendar and one might therefore expect that they would have lost some of the originality that they undoubtedly had in the beginning. But if we look at the subjects of the Institute's symposia over the past decade we cannot help but recognize and applaud the freshness and pertinence of all of them to the contemporary scene. Some have seemingly been in response to current biological thinking, while others have anticipated a popular movement in the science. How apt, for instance, was the symposium on *The Natural History of Aggression* which had papers presented by people of Lorenzian calibre at a time when animal and human behaviour studies were at their height and were soon to be fascinating a wider public: then again, when the pesticide problem was coming into public prominence with all its attendant confusion, the Institute chose as its symposium's theme *The Problem of Birds and Pests.*

Through these ten years or so the Institute has managed to provide a timely focus for some of the chief biological problems of our time and because of this it has helped greatly to get matters into some sort of perspective. In my opinion the two most important of the symposia are the last two, *The Optimum Population for Britain* and the subject of the present volume *The Future of Man.* It is an example of the timeliness of these now famous symposia that this one in particular should have been held a year before the United Nations Conference on the Human Environment and further that the papers should be published in the same year of the Conference. One could almost say that, taken together, all the Institute's symposia would have made an excellent guide to those whose work it was to organize that United Nations Conference.

In *The Future of Man* the Institute of Biology has, as it were, arranged some peculiar bedfellows between its sheets, but they do represent a wide range of viewpoints of a problem. Of course all the papers are not of equal standard or even relevance, though this could be due more to the outlook of the reviewer than anything else. However, someone once said that all things are relevant and this is presumably the philosophy of the Institute. All in all, the papers published here are worth reading, whether relevant to the general theme or not, and most are well written. One or two could have done with a little tighter editing and sometimes one gets the feeling that the selectors were trying to be a little too "with it" whereas the Institute of Biology has proved again and again that it can put together a fascinating assembly of people and views that are pertinent to our times.

ARTHUR BOURNE

Muscle

Muscle Biology: a Series of Advances. Edited by R. G. Cassens. Volume I. Pp. x+299. (Marcel Dekker: New York, August 1972.) $17.50.

THIS, the first volume of a series, is based upon lectures delivered at the Institute for Muscle Biology, Madison, Wisconsin, in the spring of 1971. The respective chapters deal with the energetics of muscle contraction (Mommaerts), muscle regeneration (Carlson), enzyme kinetics (Taylor and Lymn), force-velocity relationships in heart muscle (Brady), muscle growth and atrophy (Goldberg), the effect of adrenergic neurotransmitters on the uterus (Marshall), spindle structure and function (Smith and Ovalle), muscle changes resulting from motoneurone dysfunction (Engel and Warmolts), the histopathology of human and chicken muscular dystrophy (Shafiq, Askanas, Asiedu and Milhorat) and oxygen uptake by striated muscle (Stainsby and Barclay). Each chapter gives a well-referenced review of current knowledge, and even though the book has been produced by a photo-offset method of reproducing typed manuscripts, the illustrations, which include a number of electron micrographs, are in general clear and of good quality. As is inevitable in any such multi-author work, the individual chapters vary considerably in scope but all contain material of considerable interest to biologists and to all who are interested in disease and dysfunction of cardiac and skeletal muscle. That by Smith and Ovalle, which occupies some eighty pages, is a particularly comprehensive survey of the structure and function of intrafusal muscle fibres. The appearance of subsequent volumes in this series will be awaited with interest; it is unfortunate that a book produced by a method designed to ensure rapid publication has taken so long to appear; one hopes that the editor and publisher will try to see that succeeding volumes are published more rapidly, as this is a field in which knowledge is advancing rapidly.

JOHN N. WALTON

Drug Problems

Dealing with Drug Abuse: a Report to the Ford Foundation. Pp. x+396. (Macmillan: London and Basingstoke, June 1972.) £3.95.

IT would seem quite difficult, given what is known about drug-taking in America, to prepare a concise and reasonably objective description of the priorities for further research into treatment of drug users, public education in the field, and other relevant aspects of government policy. The *Summary of Findings, Conclusions, and Recommendations* (of the Drug Abuse Survey Project, financed by the Ford Foundation) provides just such a description. The present volume contains the Summary by Patricia M. Wald and Peter Barton Hutt) and seven staff reports.

The large existing literature notwithstanding, relatively little is known about how the various psychoactive drugs work nor about their long-term psychological and physiological effects. There is a particularly great need for interdisciplinary research (for example, relating the pharmacological and other effects to various social environments), study of the interaction of different drugs taken in combination, and experimentation with heroin use and maintenance.

The pharmacological literature on psychoactive drugs is summarized in a paper by James V. DeLong.

The second staff paper is a descriptive listing of drug education programmes, compiled by Patricia M. Wald and Annette Abrams. The main reported difficulty is a failure to evaluate suitably —or even to develop adequate criteria for evaluating—the very large number of efforts.

A paper by DeLong on treatment and rehabilitation is devoted largely to programmes for heroin users. Of various alternatives (for example, civil commitment, therapeutic communities, opiate antagonists), methadone maintenance programmes appear to be having the greatest overall "success".

"The Economics of Heroin" (by John F. Holahan) includes a description of international sources of supply and the likely effects in America of various alternative policy decisions.

A straightforward account of federal expenditures on drug-abuse control is provided in a staff paper by Peter Goldberg and DeLong.

Probably the most important and innovative paper is by Andrew T. Weil, "Altered States of Consciousness". The investigator begins with a clear summary of the relationship (or lack thereof) between the pharmacological and social/psychological effects of various classes of drugs. He then points out that drug experience can best be understood in terms of altered states of consciousness, and he lists four proposals "to be kept in mind as the direction to move toward": recognition of the importance of altered states of consciousness and the existence of a normal drive to experience them; provision for the experience of altered states of consciousness in growing children; incorporation of the experience into society for positive ends; and encouragement of individuals to satisfy their needs for altered consciousness by means that do not require external tools.

The final staff paper, by Edgar May, provides a description and tentative evaluation of the British "system" of opiate-prescribing clinics. The treatment of addiction by medical rather than law enforcement procedures is speculatively regarded as having prevented a problem such as is seen in the United States.

HERBERT H. BLUMBERG

Origin of Spectral Lines

Radiation Transport in Spectral Lines. By G. Athay. Pp. xiii+263. (D. Reidel: Dordrecht, 1972.) 41 florins.

THIS book is one in a series of monographs which will each cover "a well defined and limited area of geophysics or astrophysics". Appropriately, this first volume is concerned with the fundamentally important area of energy transport processes and physical phenomena giving rise to spectral lines, and with methods used for extracting information concerning the medium in which the lines are formed.

In the introductory chapter the author suggests that spectral line studies in astrophysics may be divided into three phases. In the present phase, which resorts largely to numerical techniques for solving the radiative transfer equation, it is no longer necessary to suppress some of the physics of line formation in the interests of simplicity as is characterized by the earlier algebraic approach. Thus the detailed interplay of the different physical mechanisms involved in line formation is emerging and the information derived from spectral line studies is becoming more meaningful.

Much of the material presented is the result of computational work, a great deal of which has been done by the author and his colleagues. The book is to be regarded as a state-of-the-art progress report which, the author hopes, will be superseded by a treatise providing a more acceptable level in the ratio of physical insight to numerical results. The usefulness of the monograph is that it provides a valuable summary of some recent accomplishments in radiative transport problems and a guide to the directions for further research.

B. BATES

CORRESPONDENCE

Forestry Policy

SIR,—I would like to correct and put into proper perspective some of your statements about the Forestry Commission and its work (*Nature*, **241**, 77; 1973). You assert, on the basis of the case presented in the consultative document *Forestry Policy*, that forestry is an "industry whose commercial value is zero or even less" and that "the scale of the Forestry Commission's research programme is an affront". Two main issues are raised—the commercial profitability of forestry in Britain and the nature and scale of research to be carried out by the commission.

First, with regard to what you describe as the commission's "pigheadedly bullish view of the scale of operations" it must be emphasized that the commission is not an independent body but simply an instrument of government policy, dependent on the three forestry ministers for instructions as to major objectives and the size of its planting programmes. Historical events have quite properly led the government to give the Forestry Commission different objectives at different times since it was established in 1919.

Forestry Policy does not make sufficiently clear the distinction between returns from investment in new planting compared with returns to be expected from exploitation of existing forest resources, including all the capital investment in the form of land, roads, drainage, fencing, and so on, which will persist for many years. As most of the Forestry Commission's new planting has taken place since 1948, the forests are still very young and as yet only a quarter of them are in production. Consequently, in order to estimate the rate of return on investment it is necessary to make assumptions about future levels of production, costs, and prices and to assign values to the social and environmental objectives which are difficult to express in money terms. We can forecast future production with some confidence, but clearly future costs and prices are less predictable. The cost/benefit study assumed constant 1972 costs and prices, although some authorities believe that the real price of wood will continue to rise following the historical trend. No attempt was made to quantify the human, the social and the environmental benefits from forestry apart from the provision of employment and benefits to recreation.

On the assumptions mentioned above, new planting in Britain can earn up to 3 per cent, a rate which is generally higher than that obtained in other countries in temperate regions of the Northern Hemisphere. When one considers the continuing management of the existing forest estate, the financial returns are estimated to be much higher, probably of the order of 9 per cent. It is estimated that at current prices the revenue from the timber which will eventually be harvested from forests, which as you state have cost £405 million, will be about £1,000 million. (The eventual value of the timber should not be confused with its discounted value.) Although the discounted value of the harvested timber will be less than the cost of £405 million, this is a reflexion of the fact that forest investment from the time of inception in 1919 has been charged a rate of interest on the capital advanced which is greater than the actual rate of return to be expected from new forests in the northern temperate zone, although this return will eventually be positive.

The editorial argues that because of the commercial unprofitability of forestry in Britain, the scale of the commission's research programme is unjustified. However, regardless of the profitability or otherwise of forestry, so long as it continues on an extensive scale there will be a need for research and development to achieve increased efficiency. I should point out that only some 75 per cent of the research division's expenditure relates directly to research and development—the balance being devoted to service-type work including publications, statistical and photographic services, seed supply and advisory and consultative work for management.

There are great opportunities for improvement of timber production and cost-effectiveness by planned research, and it is noteworthy that much of the present effort is directed to existing forests and their management. Also, much of the research is now proving to be of great value in relation to planning and conservation interests, landscaping and recreation management, and to planting and management of trees in the countryside as a whole.

The editorial article asserts that the research programme of the Forestry Commission remains "scandalously immune" from the application of the Rothschild principles. In fact, for many years a major feature of the commission's research and development programme has been the close liaison between research personnel and forest managers in both the national and private sectors—a relationship that is envied by the forest departments of many other countries. In very few countries of the world is current practice so closely related to research findings as is the case in Britain. With few exceptions, the research is directed to practical ends and often consists of technical development aimed at solving immediate problems. Thus, I believe that the relevance of the commission's research and development, and its impact on practice, are attributable to a linkage with management which accords well with the Rothschild principles.

Your comment that the work on genetics, physiology and pathology has little relevance to the immediate future is ill-informed. It should be apparent from the annual report on research that the pathology programme is concerned with immediate and pressing problems including, for example, Dutch elm disease and butt rot; the physiology programme is much concerned with speedy propagation of improved clones and problems of root growth relating to the vigour and wind stability of trees; and its genetics programme is largely a practical process of selection and breeding for better form and vigour. The statement that much of the Forestry Commission's research programme is concerned with the collection and testing of seed and the improvement of germination is incorrect since in fact it accounts for less than 1 per cent of its research expenditure.

Looked at in retrospect, the commission's research work has an outstandingly good record in terms of its relevance to practice, and a considerable part of the credit for the achievements of British foresters in enabling degraded soils to support a production crop, in the successful choice of species, and in improved protection and production techniques must go to the research on which they are based.

Possibly it is the immediate practical relevance of the commission's research which led you to refer to parts of the programme as "hum-drum". If so, the commission need make no apology. Ironically, the commission's research programme has, in fact, sometimes been criticized for giving too much weight to the solution of immediate practical problems and paying insufficient attention to long term basic research, which led the Trend Committee to recommend that more basic forestry research should be carried out by a research council. This recommendation has been put into effect with the establishment of the Natural Environment Research Council's Institute of Tree Biology. It would seem singularly inappropriate, therefore, to suggest now that the "more interesting" parts of the Commission's own research programme might be transferred to the research councils. Moreover, such transfer could hardly be justified on the grounds that the research councils are commercially profitable.

Yours faithfully,

PHILIP WAREING

Department of Botany and Microbiology,
University College of Wales,
Aberystwyth

These arguments are not compelling.

(1) Professor Wareing's suggestion that existing forests would be commercially profitable if the capital cost of their formation had been saddled with an interest rate equal to the expected rate of return from new planting does not invalidate the assertion that this rate of return is much less than that expected from other forms of public investment, by which test the Forestry Commission's operations are unequivocally unprofitable.

(2) On the scale of the Forestry Commission's research programme, the question raised in *Nature* was whether a research programme costing 8 per cent of the commission's annual operating budget is justifiable when there is no prospect that research and development will make the publicly owned forests commercially viable in the ordinary sense.

(3) It is true and was acknowledged that much of the research is relevant to other aspects of British life, but the question is whether, in those circumstances, the appropriate customer (in Rothschild's sense) should be some other organization than the Forrestry Commission.

(4) Humdrum was not intended to apply to the practical work of the research division of the Forestry Commission but to such projects as the attempt to quantify the recreational benefits of British forests, referred to in the leading article of which Professor Wareing complains.

Editor, *Nature*

Addendum

A NOTE in proof should have been added to the article "Action of Black Widow Spider Venom on an Aminergic Synapse" by S. G. Cull-Candy, H. Neal and P. N. R. Usherwood (*Nature*, **241**, 353; 1973) as follows: "N. Kawai, A. Mauro and H. Grundfest (*J, Gen. Physiol.*, **6**, 650; 1972) have recently shown that BWSV also acts on lobster nerve-muscle synapses, thus confirming our report of the action of this toxin on non-cholinergic systems".

Erratum

IN the article, "Further Investigations of the Transfer of Bomb ^{14}C to Man", by D. D. Harkness and A. Walton (*Nature*, **240**, 302; 1972), the following corrections should have been made. Paragraph 1, line 7, should read ". . . differed significantly from . . ."; paragraph 5, the equation should read ". . . $D_t = 0.95\ A_t + 0.05\ O_t$"; paragraph 5, lines 8–10, should read "It seems that the finite turnover time for carbon in the human body can be measured via the temporal changes in environmental ^{14}C concentrations"; paragraph 7, penultimate sentence, should read "Smaller variations in the ^{14}C concentrations in individual soft tissues, although statistically not significant, do appear to be real".

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Local Government Boundary Commission for England—Report No. 1. (Cmnd. 5148.) Pp. vii+217+10 maps. (London: HMSO, 1972.) £1.30 net. [2211

Report of the Agricultural Research Council for the year 1971–72. Pp. vi+68. (London: HMSO, 1972). 47p net. [2411

Medical Care in Developing Countries. Pp. 40. (London: Office of Health Economics, 1972.) 25p. [2411

London and Home Counties Regional Advisory Council for Technological Education. Science Education in the Region, 1972/73. Pp. 52. (London: London and Home Counties Regional Advisory Council for Technological Education, 1972.) 50p. [2411

Government Statistical Service. Statistical News No. 19: Developments in British Official Statistics. Pp. iv+48. (London: HMSO, 1972.) 30p net. [2411

National Children's Bureau. Ninth Annual Report, 1971/1972. Pp. 43. (London: National Children's Bureau, 1972.) [2411

The International Commission on Radiological Protection. ICRP Publication No. 18: The RBE for High-LET Radiations with respect to Mutagenesis. (A Report prepared by a task group of Committee 1 of the ICRP.) Pp. iv+45. (Oxford and New York: Pergamon Press, 1972. Published for ICRP.) £1.50. [2411

Royal Observatory Bulletins. No. 171: Computer Programmes for Differential Curve-of-Growth Analysis. By A. L. T. Powell. Pp. 1–24. 35p net. No. 172: The Allocation of Objective Gratings to Faint Star Photometry. By G. A. Harding, R. S. Harbour and K. P. Tritton. Pp. 25–60+3 plates. 65p net. No. 173: An Abundance Analysis of Alpha Centauri. By Valerie A. French and A. L. T. Powell. Pp. 61–104. 60p net. (Herstmonceux: Royal Greenwich Observatory, 1972.) [2411

Reading University Geological Reports, No. 5: A Collection of Computer Programs in Basic for Geology and Geophysics. By Roger Till, David T. Hopkins and Clive McCann. (Reading: Geology Department, The University, 1972.) 50p. [2711

The Geological Record. 1968, Vol. 105, Section 14: Protochordata together with Pogonophora, Enteropneusta, Graptolithina, Pterobranchia and Phoronidea. Compiled by D. B. Carlisle and R. O. Connick. Pp. 45. 1969, Vol. 106, Section 2: Protozoa, Part 1 (Recent) and Part 2 (Fossil). Compiled by the Staff of the Zoological Society of London. Pp. 214. £8; $19.30. 1969, Vol. 106, Section 3: Porifera. Compiled by S. Ware. Pp. 19. £3.50; $8.50. (London: Zoological Society of London, 1972.) [2711

Koch-Light Laboratories, Ltd. 1973 Catalogue. Pp. 583. (Colnbrook, Bucks: Koch-Light Laboratories, Ltd., 1972.) *Gratis*. [2711

At the Famers' Service: A Handy Reference to Various Services Available to Farmers in England and Wales. Pp. 79. (Pinner, Middlesex: Ministry of Agriculture, Fisheries and Food, Tolcarne Drive, 1972.) *Gratis*. [2811

Concorde: Ten Years and a Billion Pounds Later. By Chris and Liz Edwards. Pp. 46. (London: Pluto Press for the Anti-Concorde Project, 7 Chalcot Road, NW1 8LH. 1972.) 30p. [3011

University of Nottingham, School of Agriculture Report 1971–1972. Pp. 132. (Sutton Bonington, Leicestershire: University of Nottingham, School of Agriculture, 1972.) 60p. [3011

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Chronic Currency Crisis Continues

THE latest bout of uncertainty about the stability of the international currency system has now been temporarily resolved by yet another adjustment of parities. Next will come more concessions to the United States on the restriction of international trade and a still further complication of the rules that govern the international money market and in particular the still further elaboration of the attempt to distinguish between commercial and capital transactions of the kind now embodied in their purest form in the two-tier system operated by the French. Nobody will expect that the new arrangements will last very long. It has taken just over twelve months for the Smithsonian Agreement to collapse. But the prospects for the future are not especially bright. The restrictions on imports maintained by the Japanese government will no doubt continue, in flagrant violation of the spirit if not the letter of the General Agreement on Tariffs and Trade. The United States will no doubt be edged in the same direction by the uncertainties of the past few weeks. And there is still no sign that the European Community is in a position or even a mood to create the financial institutions without which the concept of a European Community is incomplete.

What is to be done? The first need is that there should be a concerted attack on the Japanese position. The remarkable growth of the Japanese economy in the past few years is entirely a consequence of the way in which the Japanese export trade has flourished and thus of the willingness of countries elsewhere to import Japanese goods freely. During 1972, nations such as the United States and Britain, anxious to reduce the resulting drain on their balance of payments, have attempted to persuade the Japanese government to induce Japanese exporters to adopt voluntary restrictions on their export trade, but this expedient is at once unworkable and less satisfactory than a thorough liberalization of the rules by means of which the government of Japan ensures that it remains in surplus with its trading partners. But since Japan has every interest in being in the international swim, it is surely a simple issue of international diplomacy that there should be a further and rapid liberalization of Japanese trade. Whether the result would be, as the United States would hope, an immediate rectification of the adverse balance of United States trade is however doubtful—what the Administration has to acknowledge is that the effective devaluation of the dollar in 1971 and that now in effect have been brought about by the changed balance of prosperity between the United States and the other advanced countries of the world which has become apparent in the past decade.

Where the European Community is concerned, the immediate need is to develop machinery not merely for forming a common financial policy but for broadening the base within which such a policy is worked out. At the Paris Summit meeting last year, the nine members of the European Community paid lip service to the view that by the end of the present decade there should be a common monetary system, which implies not merely a common unit of currency but the financial institutions needed to back it up and, more important, a measure of permanent agreement on the equitable distribution of resources within the European Community. In other words, before a monetary union is possible, the member countries of the European Community will have had to agree on a common policy for the support of social services, including the arrangements for paying unemployment benefits to those who are out of work. There will have to be a common regional policy and machinery for economic planning at least in the broad sense of determining the steps which need to be taken to ensure an equitable distribution of industry and of jobs within the nine member states.

Currency crises are either calamities or opportunities according to the mood of those who must deal with them. Formidable though the obstacles to economic integration in Europe may be, one of the disappointments of the past week's negotiations is the apparent lack of an explicit recognition that the edge might be taken off the problem of currency instability by accelerating the timetable provisionally agreed in Paris for economic union. On the face of things, it would have done no harm at all if Mr Anthony Barber, the British representative at last week's Paris meeting, had advocated that the timetable for economic union should be advanced to, say, July 1974. Although there are formidable issues to be settled, what needs to be done is clear enough and the European Community has in the past made progress chiefly by setting itself apparently impossible timetables and then staying up all night to meet them. And in the present situation, anyway, the whole concept of the European Community will be incomplete until these radical issues are decided. Indeed, the arrangements which the community is trying to force on its members for the regulation of currency transactions themselves contain the seeds of further instability. Currencies are meant to move only narrowly against each other, and the British government has promised that the floating pound will eventually be fixed. But how can such a system survive the inevitable imbalances of trade among the members of the European Community if there is no mechanism for making sure that countries which run a deficit on their trading balance are somehow helped to make up the difference? It follows that the members of the European Community should hurry to settle their internal arrangements for exchanging currencies in case they find they have built into their internal arrangements the kind of instability which has now emerged internationally. It is unthinkable that the present system can survive until 1980 and the sooner European governments acknowledge that the better.

Decisions in Secret

THE Post Office believes that it has learned two lessons from its own history. The first is not to put all its eggs in one basket; the second is to disguise big decisions so that they cannot later be said to have been wrong. For the switching system for the British telephone network in the years immediately ahead, the Post Office has, after long deliberation, decided to order the controversial TXE-4 reed-relay exchange. But it will not order nearly as many as it might have done. At the same time, it will increase by tenfold its purchases of crossbar exchanges (which advanced telephone systems in other countries now rely on), so that crossbar will actually outweigh TXE-4 in the system to a considerable degree. And there will be more orders of the smaller TXE-2 exchanges which, like the TXE-4, depend on reed relays to make their electrical contacts. This mixed package will bridge the gap between the antiquated Strowger step-by-step switching on which Britain's telephones deplorably now depend and the electronic, solid-state, digital, computer-directed exchanges of the future.

This mix has been specially designed to placate the Post Office's three major suppliers, Standard Telephones and Cables, GEC, and Plessey. STC has been producing TXE-4s—16 of them under an initial contract worth £15 million. But the other two, Plessey particularly, were not keen to follow suit. They have seen the TXE-4 as a stopgap invention, eccentrically British, of little export value. The Post Office would probably have liked to nominate the TXE-4 as the standard large (over 10,000 lines) exchange for the next few years but it would have done so at the risk of offending Plessey and also of making a conspicuous major error.

But is the decision the right one for Britain? The Minister of Posts and Telecommunications, Sir John Eden, will have to give his approval before it is made final. Sir John appreciates the gravity of his action, about £1,300 million is to be spent on telephone exchanges over the next five years and the present state of the service is sad and the long waiting lists of would-be subscribers are a political embarrassment. But who will advise him —if not the Post Office and the three suppliers most concerned?

Such important choices and the debates that precede them should be made in public. The fact that the details are technical and tedious to the ordinary politician, let alone the man in the street, is irrelevant. There are a great many technically literate people around and a great number of companies (one must remember that they need not all be British) which might have technical and commercial solutions to offer on Britain's telephone dilemma. Their views should be heard. Sir John Clark, chairman of Plessey, worked hard to dissuade the Post Office from too heavy a reliance on the TXE-4 and apparently he succeeded. But should not such experts from vested interests give their advice to the Post Office in the knowledge that it will be open to criticism from those outside the Post Office?

The uncertainties over the TXE-4 are not hard to resolve. People at STC are confident that it has export potential, that it is the best possible bridge between Strowger and an all-electronic system and that it can be modified, as the telephone network is modernized, to include solid state technology. But had the deliberations been open, people might have been reminded, as they certainly have not, that the TXE-4 will not give telephone users any of the new services like abbreviated dialling, calls recorded at the exchange if the subscriber is out, and automatic transfer to calls to another number that are becoming available in Canada and the United States.

The TXE-4-crossbar compromise has been secretly arrived at and it has done little to create the needed new relationship between the Post Office and industry on research and development. Moreover, it seems to have been conducted with hardly a mention of the word Europe, even though the European Economic Community intends that there should be an all-European integrated telephone network by the 1990s, with a true common market in supplies of communications equipment.

Euratom Soldiers On

THE best thing to say about the agreement between the European governments reached in Brussels on February 6 about the future of Euratom is that it provides a tangible programme for the next three years. Uncertainty is good for nobody and the uncertainty which has plagued the four joint research laboratories for almost five years has been especially damaging to the staff. So far, so good. But it remains something of a mystery to know whether the compromise at Brussels will do much more than postpone the question of what should be done about the four laboratories which are in practice the only tangible legacy of the ambitious plans for a coordinated European research programme in nuclear energy mapped out by Euratom in the 1950s. Where nuclear fission is concerned, the joint research laboratories have only an insubstantial contribution to make to the development of practical power stations—their experimental and test reactors, for example, contribute nothing of substance to the devices which are available elsewhere, while there is no prospect that the joint research laboratories will be able to recapture the opportunity for coordinating development on schemes such as those for fast reactors now being pursued independently, and with very little collaboration, in Britain, France, Germany and Italy. On fusion, the laboratories have a potentially more valuable part to play, but even here the sceptics can fairly say that even this opportunity will be lost before another three years have passed.

What might be done? A coordinated policy on fusion research is necessary and it would be in everybody's interest if the several governments with a finger in the pie would at least explore the possibility that Euratom might become a coordinating authority. At the same time, however, it might be recognized that Euratom has very little more to say or do about fission reactors, but that there is a need—an urgent need—for a better articulation of national research programmes on fast reactors and that Euratom might act as a kind of secretariat for that process. For the rest, it should be acknowledged that the best use of the staff that Euratom has accumulated would be to serve as extra manpower for the national laboratories already doing useful work in fields where European integration is inevitable — in standards and metrology, for example. The fact that the new budget for Euratom does provide for the transfer of Euratom staff to national laboratories is in this sense an advantage. In the period between now and April, when the European Commission is required further to define the research programme, and in the two years between now and the next review of the programme, urgent steps should be taken to see that schemes like this are thoroughly explored.

Pipeline in Trouble

THE chance that the United States will be able to reap the benefits of the vast oilfields on the North Slope of Alaska continues to recede. A week ago, the United States Appeals Court astonished all parties to the project to build a pipeline from the North Slope to Prudhoe Bay —the consortium of petroleum companies, the disputant environmental groups and no doubt the US Department of the Interior as well—by ruling that the department has no authority to grant a permanent right of way across federal lands to those who would have to service any pipeline that might be built. It is, of course, astounding that the Department of the Interior should have been caught out on a technical legality like this. The result will be that if the department can summon up the nerve, Congress will have to be invited to change the law, in circumstances in which it will be impossible to separate the strictly legal argument from the wider environmental arguments which have bedevilled the Alaskan pipeline almost from the start. Although it is quite fair that complainants should have protested, at the beginning, that the petroleum companies were willing to push ahead with the pipeline project with only scant concern for environmental considerations, more recently it would have been more proper to complain that the Department of the Interior has been a pusillanimous arbitrator in the dispute, and reprehensibly slow to give a lead.

What should it now be urging? The legal argument quite apart, the urgent need is for the department to decide just what contribution the North Slope can be expected to make to the supply of energy in the United States. And if, three years ago, the department's opinion on the virtues of the pipeline project was evenly balanced—the more charitable interpretation of its equivocation—the recognition of the petroleum shortage in the past six months must surely have tipped the balance in favour of exploitation. Surely it will be a strange situation if the United States now shoulders the burden of paying up to $50,000 million a year for imports of oil from the Middle East and at the same time decides to leave the petroleum beneath the North Slope where it is. It will be stranger still if the United States permits an increase in the price of petroleum, which could easily double in the next few years, while imposing on itself a self-denying ordinance where Alaskan oil is concerned. Nobody will pretend that the environmental arguments against the Alaskan pipeline should be brushed aside, but at some point in the next few months the United States will have to recognize that some at least of what it now calls the energy crisis is the price which it has chosen to pay for leaving Alaskan oil alone.

At the same time, the United States must somehow come to grips with the problem of putting a value on the environmental qualities which it has come to revere. A part of the argument against the pipeline is that it will permanently disturb a unique ecological system, and that is a point that does require further investigation and consideration. At the same time, a part of the United States environment to which many American voters are attached is that part of the social fabric which provides them with warmth in the winter, air-conditioning in the summer and the power needed to keep American industry in being. An accurate decision about the Alaskan pipeline requires not merely that there should be an investigation of what the environmental damage will be, but an open public discussion about the damage should be weighed against the cost either of importing fuel from the Middle East or of doing without it. Unhappily, there is no real assurance that Congress will be the right forum for making this choice.

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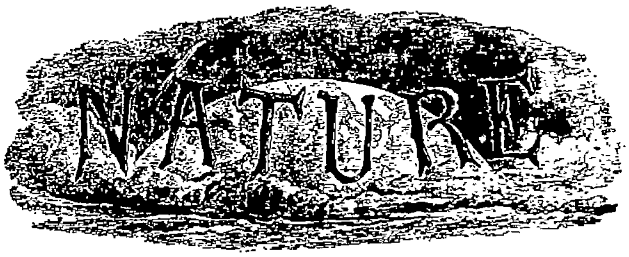
100 Years Ago



Inherited Feeling

THE remarkable case of an inherited feeling of dislike for a special class of persons, communicated by Mr. Darwin, appears to me to support a view I have long held (but not yet published) as to the explanation of another class of so-called instincts. The three separate instances given in which the dogs showed a violent antipathy to butchers, either without seeing them or when they were dressed as gentlemen, clearly indicates that it was through the sense of smell that the painful sensation was experienced; and this is quite in accordance with the wonderful delicacy and importance of this sense in most animals, and especially in dogs. It is natural to suppose that some ancestor of these dogs was systematically and cruelly ill-treated by several butchers, perhaps from some thievish propensity or other bad habit which required frequent punishment, so that the smell of a butcher came to be invariably associated with pain and a desire for revenge. But the most important fact to observe is, that there must be some peculiar odour developed in human beings by constant contact with flesh, which a dog can recognise apart from individual peculiarities and in spite of perfect disguise. Now the power many animals possess to find their way back over a road they have travelled blindfolded (shut up in a basket inside a coach for example) has generally been considered to be an undoubted case of true instinct. But it seems to me that an animal so circumstanced will have its attention necessarily active, owing to its desire to get out of its confinement, and that by means of its most acute and only available sense it will take note of the successive odours of the way, which will leave on its mind a series of images as distinct and prominent as those we should receive by the sense of sight. The recurrence of these odours in their proper inverse order—every house, ditch, field, and village having its own well-marked individuality—would make it an easy matter for the animal in question to follow the identical route back, however many turnings and cross-roads it may have followed. This explanation appears to me to cover almost all the well-authenticated cases of this kind.

ALFRED R. WALLACE

I HAVE a cat, of a long-haired breed, whose aversion to dogs is unusually strong. Last autumn, six kittens of hers, under two days old, were in a corner of the kitchen where they had had no opportunity of making acquaintance with any dog; yet, on being stroked (in their mother's absence) by a hand which a dog had just licked, more than one of them "swore" violently. This was repeated several times, but the little creatures showed no dislike to being touched with a clean hand.

A LOVER OF ANIMALS

From Nature, 7, 303, *February* 20, 1873.

Further Support for Post-Apollo Project

BRITAIN and the Netherlands have joined the post-Apollo programme. In the past week both countries have agreed to join the European Space Research Organization's studies of the post-Apollo sortie lab and ESRO has awarded the final study contracts.

Announcing Britain's belated entry to the fold, Mr Michael Heseltine, Minister for Aerospace and Shipping, said that he had offered ESRO a contribution of £300,000 to the phase B 2 studies. Work on this, the final stage of ESRO's three part study of the technical and financial requirements of the sortie lab, start this month and will run until August. The United States has set mid-August as the deadline for ESRO to reach a decision on whether it is actually going to build the lab for NASA.

But Mr Heseltine made it clear that Britain's commitment is limited. "The UK is in no way committed to participate in further stages of the studies or in subsequent development and construction stages," he said in parliament last week.

In fact Britain has offered ESRO ten per cent of the phase B study costs, or £300,000, whichever is the smaller. The contribution is effectively backdated as it covers the phase B 1 studies which began in November and ended last month. The total cost of phase B is put at 7.5 million units of account (about £3.1 million).

Meanwhile ESRO has announced that Erno VFM-Fokker and MBB, two West German companies, have been awarded contracts worth 1.4 million units of account each, to handle the phase B 2 work.

It is a condition of the contracts that the companies sub-contract so that each participating states receives a proportion of the work related to its contribution to the programme.

Six of ESRO's nine member countries have now agreed to participate in the studies. The original four, Italy, Belgium, Spain and West Germany, agreed to foot 20 per cent, 4 per cent, 3 per cent and the remainder of the bill respectively. The addition of Britain and the Netherlands will reduce West Germany's share of the cost from 73 per cent to about 60 per cent.

ESRO, now that its "special project" to develop the sortie laboratory is established (see *Nature*, **241**, 302; 1973), is committed to developing it, although the individual countries (witness Mr Heseltine's statement) are not. There is, however, an escape clause which states that the organization can withdraw if by mid-August it finds that the cost of the project will "unacceptably exceed" the original rough estimate of $250 to $300 million. Care has been taken not to define what "unacceptably exceed" means.

The object of the final studies is, as far as possible, to fix the costs and to "establish the configuration (of the unit) in the light of user requirements". The laboratory is expected to consist of two parts. A pressurized manned laboratory and an external unpressurized instrument platform, known as the pallet, intended for research activities on shuttle missions lasting seven to thirty days.

The laboratory will house experimental apparatus data processing equipment, electrical power equipment and crew control stations. The staff, of up to six scientists and engineers, will eat and sleep in the shuttle orbiter, but will be able to work in the laboratory in "normal shirtsleeve conditions", as NASA puts it. The pallet will have large instruments such as telescopes and antenna mounted on it, and experiments will be remotely controlled from the laboratory. The whole unit will remain attached to the shuttle throughout the mission.

If all goes well and ESRO and its member states decide to proceed with development and construction later this year, NASA should receive the first unit in 1979.

SCIENCE POLICY

Research after Rothschild

Now that the dust has settled on the great debate on reorganization of government research and development, Sir Alan Cottrell, who was at the heart of the debate, attempted last week to put it in its proper perspective.

Research and development, said Sir Alan at the annual dinner of the Parliamentary and Scientific Committee, is "only a small part of the total scientific and technical activity of the country". Sir Alan cited the scientists who are in management and sales, the weather forecasters, operational analysts and many others who provide scientific services to the government, as being part of the government science machine, but who were not directly affected by the green and white papers.

Britain has had many scientific and technical successes recently, said Sir Alan, the advanced passenger train, new techniques of weather forecasting and the development of equipment for the dispersal of oil at sea being just a few examples.

But now is not the time for Britain to rest on its laurels and closer understanding is needed between the researcher and the user, which, said Sir Alan, "is one of the reasons for our reorganization".

But Britain's efforts must not be spread too thinly—the requirements boards, for one thing, will ensure that this does not happen—and "we must . . . not embark on glamorous and costly developments simply because they are fashionable". The answer in certain instances will lie in collaboration with our partners in the European Economic Community.

One of the basic problems that Britain faces is that of generating sufficient investment capital—a problem which is likely to become more severe in the coming years. But massive investment brings other difficulties, said Sir Alan, the major ones being possible inflation and balance of payments problems.

There is no worry, in the scientific sense, that material resources will be exhausted, but the price will increase, says Sir Alan. There will, therefore, be a need for improved techniques of mining and scrap recovery, and recycling will have to be intensified, all of which will need considerable scientific and technical effort. The critical factor however, according to Sir Alan, will be the availability of energy to carry out the work.

Britain is well blessed at present with adequate coal reserves, North Sea gas and oil, and nuclear developments. But Sir Alan feels that this is no time to feel complacent, and both the coal and nuclear industries must plan vigorously for the future. Parallel efforts must also be made to use energy resources more efficiently and economically.

The full text of Sir Alan Cottrell's speech will be published in *Nature* soon.

CLUB OF ROME

Onwards Undaunted

from La Recherche

In spite of severe criticisms since publications of *The Limits to Growth* last year, the Club of Rome, which commissioned the report from Professors Jay Forrester and Dennis Meadows at MIT, is undaunted and embarking on several more projects designed to study other related problems, particularly those of population, natural resources, and economic growth.

At a meeting held near Paris recently, the Club unfolded its seven point current research plan. The club, true to form, is, with the support of the Volkswagen Foundation, studying the effects of doubling the world population. A second group of projects surveys the reallocation of the world's resources (with emphasis on energy, food and raw materials), and also looks at the position of Japan in world affairs. A third measures the limits to German growth, the nature of change in technical innovation and the patterns of economic development in West Africa, India and the Republic of Korea.

The rest of the study areas concern national population strategies, aspects of worldwide technological forecasting and the goals and constraints which could affect future science and technology.

A group of researchers headed by Mihajlo Mesarovic (Case Western Reserve University) and Eduard Pestel (Technische Universität, Hanover), is elaborating a computer-aided "strategy for survival", a long term multi-level world model project. The group has recently published *An Interactive Decision Stratum for the Multilevel World Model,* which is largely an econometric exercise in forecasting allowable levels of consuming raw materials and other resources. To answer criticisms made of such forecasts—that variables, representing policital, social or psychological decisions and events are missing — Pestel and his team will next attempt to quantify such factors for application to future models. This summer they hope to provide an analysis of future options in using the world's energy resources, and in a year's time they hope to have a model able to absorb the parameters of monetary erosion as it affects capital investment in the energy field. Pestel claims that this will lead to "new sets of decisions possible in the attenuation of the energy crisis and the polluting character of some present energy sources, as well as economic measures to be implemented".

Peccei, faithfully defending the club's philosophy of forecasting based on computer models, said at the meeting that "Our efforts are still too modest at the Club of Rome. The first research project we did cost exactly what all the world's military forces were spending at that time in the incredibly short span of 30 seconds!"

ATOMIC ENERGY

Krypton Needs Limiting

from a Correspondent

Means will have to be found to control the discharge of gaseous krypton-85 from nuclear power stations before the end of the century. Tritium release will also have to be controlled, particularly where local conditions are adverse, but otherwise the problem of an increase in background radiation from the use of nuclear power seems to be well under control. This was one of the chief conclusions of a conference on nuclear energy and the environment held in Liège recently under the auspices of the Association des Ingenieurs Electriciens. The meeting agreed with other conferences' findings that by the year 2000 the addition to the background radiation will be less than one per cent of present levels given the current projections of the increase in nuclear power plant.

The conference also discussed the problems of heat dispersal from power stations and came to the conclusion that by the end of the century Europe's rivers and lakes may not be able to absorb all the waste heat generated. The problem, it was felt, is acute, and must be tackled not only by the designers of power stations, but also by the politicians who plan energy programmes.

The International Commission on Radiological Protection (ICRP) was praised for its work in setting permitted levels of radiation early in the development of nuclear power.

Professor Z. M. Bacq, a biologist from the University of Liège, discussed the evidence that certain cells appear to have repair mechanisms that are effective in the face of low doses of radiation. This implies that there may be a threshold value below which radiation causes no cell damage. Dr F. D. Sowby, scientific secretary of ICRP, said that he was aware of this evidence that decreased doses of radiation do not produce a linear decrease in radiation damage, but he emphasized that until it is more clearly shown that the non-linear effect applies to man (to date it can only be uncertainly demonstrated in mice), the commission will continue to base its permitted exposure levels on the more pessimistic assumption that cell damage does decrease linearly with decreased radiation.

COMPUTERS

Eyes East

In spite of government enthusiasm for a European computer company, ICL appears to have its sights set on a Japanese rather than a European link.

International Computers Ltd, Britain's largest manufacturer, told the Select Committee on Science and Technology last week that the "ever growing strength" of the Japanese industry worried it. Cooperation with Japan might be possible, however, through Japan-ICL, a subsidiary of the British company, which at present sells non-computer equipment such as punch card sorters and output punchers in Japan.

On cooperation in Europe, the company said that "in view of ICL's evident technical strength and market share relative to the other European computer firms, any unification of the industry could most effectively be centred around ICL".

The company emphasized that any benefits that are derived from harmonization of the European computer industry must be commercial in nature, and not political. But the company was not enthusiastic about the possibilities of successful links being formed. It went on to say that "it is very doubtful in ICL's view if the benefits (resulting from recent agreements on cooperation between Siemens, CII and Philips) will be sufficiently timely or substantial to have any major impact on the relative position of the European computer industry *vis-à-vis* United States manufacturers".

Talks between ICL and Nixdorf in West Germany and CII in France have failed to produce agreements on joint development work because of "various technical and commercial problems". Exploratory talks with United States manufacturers had seemed, ICL said, to have offered "at this point of time no worthwhile commercial advantage".

ICL reaffirmed its belief that by 1976-77 it should "have reached a level of size and profitability adequate to make further research and development support unnecessary". (The government made ICL a £14 million loan last August to help develop the company's new product line.) But the company emphasized that when this support ends the government should continue to provide development contracts for specific projects as well as orders for ICL equipment.

The company's situation has not been helped by a sharp cut in computer orders from the government. In 1971 the government announced that it expected to place orders worth £20 million with ICL that year, but up to September 1972 the company had only received orders worth £18.5 million.

COMPUTER DESIGN

Closer Collaboration

Yet another call for university research workers and industrial scientists to exchange views and ideas is made in the Science Research Council's Engineering Board's report on *Research Support for Computer Aided Design* published recently.

Industry spends more than £1,000 million on design every year and the Department of Trade and Industry's computer aided design centre has estimated that a twenty per cent saving can be made in a wide range of engineering applications if the engineering industry turns fully to computer aided systems. The actual annual saving would be higher than the calculated £200 million because a switch to computer design would lead to new concepts and improved manufacturing procedures.

The report pinpoints several areas where industry would benefit from greater use of computer aided design. Traditional skills are dying in the die mould and pattern making industries and several companies are in need of new design and manufacturing techniques. The ship design industry is also a prime contender for the application of computer aided design research and the machining systems industry, according to the report, needs coordination of machine tool design, interactive aids and numerically controlled machine tools so that the industry can move more quickly into manufacturing.

The civil engineering industry is well advanced in the techniques of using computers for designing engineering systems and in integrating design products but the SRC feels that it would be prudent for the industry to now consider integrating design and production, in particular, the report says, so that selection of components, ordering of materials and the organization of work on site should be more closely integrated.

But the introduction of these advanced computer ideas into industry needs a flow of information from universities where the basic work is being done. University workers, says the report, "should be made aware that successful contact with industry requires a considerable degree of the researcher's personal time" and it goes on to say that the best means of exchanging ideas is by personal contact, provided it is supported by "adequate and appropriate documentation". Engineers from industry should be encouraged to join university research groups for periods ranging from a week up to a year.

Research in computer aided design would also benefit from a closer knitting of existing groups, especially as the subject calls out for more interdisciplinary cooperation. The research groups should, naturally, have active support from computing science departments and should be active in running post experience courses. But the report does not favour these groups having their own large computers and they should, if the need arises, install terminals connected to a central facility.

The SRC is prepared to support groups setting out to do research in computer-aided design in engineering but the report points out that SRC grants are primarily intended to supplement existing research projects. After a suitable interval the university, or institution, is expected to assume full, or partial, responsibility for the group.

Nuffield Trustees

The Nuffield Foundation, which last year awarded more than £1 million in grants, will have a new chairman managing of trustees in April. Sir Geoffrey Gibbs, who has been at trustee since the foundation was set up in 1943 and chairman since 1951, is retiring and will be replaced by Lord Todd, who has been a managing trustee since 1950. Professor Hans Kornberg, who holds the chair of biochemistry at the University of Leicester, was made a trustee of the foundation on January 1 and will fill the breach caused by Sir Geoffrey's retirement.

WEATHER RESEARCH

US/USSR Cooperation

from our Soviet Correspondent

A joint Soviet–United States research expedition to the Bering Sea was inaugurated on January 31, 1973, with the sailing of the Soviet weather ship Priboi from Zolotoi Rog bay, near Vladivostok. In addition to the Priboi, the Soviet team is supplying an Il-18 aircraft equipped as a flying laboratory, while from the American side NASA is providing an icebreaker and an aircraft.

A two-month research programme is planned, which will study the surface of the sea in various temperature conditions, the physical and chemical parameters of sea water, the density and growth of ice and the content of water vapour in the atmosphere. Measurements made from the ships will be compared with data on microwave reflexion from the sea and ice surfaces, recorded by the aircraft.

The programme has been designed under the terms of the 1972 agreement between the Soviet Union and the United States on cooperation in the exploration and use of outer space for peaceful purposes; although no specific mention has been made of satellite data, it would seem that the readings obtained by the Bering expedition will also be compared with those of weather satellites. The material gathered by the expedition is intended for use in the development of weather forecasting methods for Arctic and sub-Arctic waters.

CRIMOND TERMINAL

Surveys Continue

Total Oil Marine is undertaking further surveys of the east coast of Scotland to examine alternatives to the Crimond site for the gas processing plant needed to handle the output of the Frigg gas field.

The disused airfield at Crimond on which Total and the British Gas Corporation want to build the processing plant lies alongside Loch Strathbeg, which is classified as of grade one scientific importance by the Nature Conservancy (see *Nature,* **240**, 435; 1973).

At a meeting in the Buchan village of Crimond last week, Mr David Wood of Total revealed that the coast had only been examined in detail from Fraserburgh to Rattray Head—a distance of a little over eight miles—but added that further surveys are in progress. This week Mr Wood said that "we are taking a complete look at the whole thing, both offshore and elsewhere". Results, he said, "are expected in weeks rather than months".

The reason for continued surveys, Mr Wood says, is that the Ministry of Defence already has planning permission to use the land for a radio station. If and when the decision on who is to have the land comes to a head "there is no guarantee that energy will get it over defence".

Mr Wood also concedes that it is likely that only four pipelines could be brought ashore at Crimond. Environmentalists fear that, in spite of the Gas Corporation's policy of concentrating processing plants on as few sites as possible, this might result in a second terminal being built elsewhere if a number of large gas fields are found in the North Sea.

Mr Wood says that he is not surprised by the reaction to the proposal, but he is surprised "that so many people think that they should be consulted first" and that people are "afraid that the local planning authority is likely to produce a *fait accompli*".

Mr Wood remains confident, however, that the construction of the terminal "will have no effect upon Loch Strathbeg whatsoever". "But getting the pipes to the airfield", he added, "that may be another matter".

NEW WORLD

More Ammunition for SST Foes

by our Washington Correspondent

While Concorde was still reeling from the double blows dealt by PanAm and TWA, which decided last week not to take up their options, a committee of the National Academy of Sciences has given more ammunition to the anti-SST forces. Charged with the task of examining the biological consequences of increased ultraviolet radiation reaching the Earth's surface, the committee has concluded* that "sufficient knowledge is at hand to warrant utmost concern over the possible detrimental effects on our environment of the operation of large numbers of supersonic aircraft".

Ultraviolet radiation first burst into the SST debate in 1971, just before Congress voted to block development of two prototype American SSTs. It was then suggested, chiefly by Professor Harold Johnston of the University of California at Berkeley, that oxides of nitrogen emitted into the stratosphere by SST exhausts would partially destroy the layer of ozone in the upper atmosphere. Since the ozone layer filters out some of the ultraviolet radiation coming from the sun—particularly short wavelength ultraviolet radiation—the result would be increased ultraviolet intensity at the Earth's surface which in turn would lead to increased incidence of skin cancer and other biological damage.

Dr Johnston's calculations (*Science*, **173**, 517; 1971) sparked off a scientific debate which is still essentially unresolved—in spite of a suggestion put forward in a letter to *The Times* by Sir Peter Masefield, Chairman of the British Airports Authority, which was published on January 27. Masefield stated that Johnston has admitted making a mistake in his original calculations which essentially invalidates his conclusions. Johnston said last week that such a suggestion is "quite incorrect" and that far from recanting, he has further refined his calculations and still considers his original publication a good first-order approximation.

The NAS committee, which met under the chairmanship of Dr Kendrick C. Smith, of Stanford Medical School, in spite of the general conclusion quoted above, tries to steer clear of commenting on the validity or otherwise of Dr Johnston's calculations. It simply explores their biological implications, and in so doing, brings out several points which have previously been given scant attention.

The committee starts from the premise that a small decrease of ozone concentration in the stratosphere would produce a disproportionately large increase in ultraviolet radiation reaching the Earth's surface. Particularly affected would be the amount of radiation penetrating the ozone layer with wavelengths between 286 and 320 nm, which the committee points out are "the most biologically damaging wavelengths of sunlight". A 5 per cent reduction in stratospheric ozone at 40°N—the mid-point of the United States—would increase the intensity of ultraviolet radiation at 297.5 nm by 26 per cent, while a 50 per cent decrease in the ozone layer would cause radiation at this wavelength to increase by a factor of ten. "This point", the committee suggests, "is of the utmost importance in considering the likely biological effects that might result from man-made changes in atmospheric ozone concentrations".

But since the intensity of ultraviolet radiation is reckoned to be about 50 times greater at the Equator than it is inside the Arctic circle—the difference is caused by a thinning of the ozone layer and increasing solar altitude towards the Equator—would a small intensity increase of about 25 per cent really be significant? The committee believes that it might, because not only is an average increase in exposure likely directly to affect man, but it may also be detrimental to plant life.

So far, the debate about SSTs and the environment has concentrated chiefly on the politically sensitive cancer aspect, but the NAS committee raises a number of much broader questions. It points out, for example, that ultraviolet radiation damages the DNA in all living things, but the damage is repaired by a variety of biochemical processes. The damage and repair are in delicate balance, which could be upset by an increase in average exposure to ultraviolet radiation—"if the amount of ultraviolet radiation damage exceeds the cell's capacity to repair this damage . . . then the cell will die". Moreover, since many plants and animals reduce their exposure to sunlight by behaviour responses triggered by heat or light, they may not be responsive simply to an increase in the ultraviolet component of sunlight.

Because ultraviolet radiation can

**Biological Impacts of Increased Intensities of Solar Ultraviolet Radiation*, available from the National Academy of Sciences, 2101 Constitution Avenue, Washington DC 20418.

AEC

Woman in the Chair

by our Washington Correspondent

President Nixon has finally filled one of the many top-level science positions in Washington that have been vacant as a result of reshuffling, firings and resignations that followed his re-election. As expected, he has appointed Dr Dixie Lee Ray to be chairman of the Atomic Energy Commission in place of Dr James Schlesinger, who has been made director of the CIA. A marine biologist who was appointed as an AEC Commissioner last year, Dr Ray has greeted her appointment by thanking Nixon for the honour and vowing to carry on the "forward progress" which Schlesinger fostered at the agency. Otherwise, she has kept a low profile during her six months as commissioner and has thus given few clues to her thinking on nuclear matters.

Before becoming an AEC Commissioner, Dr Ray was director of the Pacific Science Center in Seattle and associate professor of zoology at the University of Washington; her specialty was marine vertebrates. This background was expected to make her particularly receptive to environmental concerns in the commission, but so far she has made no public statements on environmental matters.

Described by her colleagues as a strong and even forceful personality, Dr Ray faces a challenging period as chairman of the commission. Not only will she have politically sensitive problems of nuclear safety and the environment to deal with, but it is likely that she may preside over the dismantling of the agency itself. The plans for reorganizing the federal bureaucracy, which President Nixon submitted to Congress two years ago, and which he has promised to resubmit this year, would have transferred the AEC's civil nuclear power functions to the proposed Department of Natural Resources. Such a move would make the commission little more than a weapons supply agency for the Department of Defense; what it would mean for the high energy physics laboratories has never been made clear.

penetrate water to depths of a metre or more, the committee suggests that the effect of increased ultraviolet intensities on aquatic plant and animal life should be carefully studied, especially in view of the importance of plankton in the food chain.

As for skin cancers, the committee points out that the three most common malignant skin tumours—squamous cell and basal cell carcinomas and malignant melanomas—are all correlated with exposure to sunlight, and quotes a calculation that "a 5 per cent decline in ozone would produce at least 8,000 extra cases of skin carcinomas and melanomas per year in a population the size of the white population of the United States".

One conclusion stands out clearly from the report, however—that the experimental basis for the committee's concerns is scanty, to say the best. The committee has therefore recommended, first, that a network of ground level stations should be established at various latitudes to monitor the intensity and wavelength distribution of solar ultraviolet radiation, to monitor possible environmental changes but also to enable proper evaluation of data on latitudinal variations in the incidence of skin cancer in man. Second, laboratory and field studies of the effects of increased ultraviolet radiation on the growth and yield of agricultural plants and on the sensitivity of plankton are urgently required. Finally, it is implicit in the report that these studies should be carried out well before a large SST fleet ploughs through the stratosphere.

ENERGY

Congress Committee

by our Washington Correspondent

The House Committee on Science and Astronautics has decided to establish a new subcommittee on energy. The chairman will be Representative Mike McCormack, a second-term Democrat from Washington State, who by-passes several more senior committee members to take charge of the committee. McCormack, who until this year was the only working scientist to sit in Congress, was chairman in the last session of a task force on energy of the Science and Astronautics Committee, the final report of which is due to be published in the next few weeks. The new subcommittee is essentially an upgrading of the task force.

Although plans for the subcommittee have not yet been fully worked out, it will probably concentrate on the research and development aspects of energy production, and it will thus take a longer term view of energy supply. Some fourteen Congressional committees now have an interest in energy.

BUDGETS

The Battle Continues

by our Washington Correspondent

The battle between President Nixon and Congress over which branch of the government should control the federal pursestrings reached boiling point last week. The focus of the disagreement is the fact that President Nixon has slashed federal spending this year by refusing to allocate some money appropriated by Congress, an action which has been regarded on Capitol Hill as usurping Congress's constitutional right to control federal spending. The White House, on the other hand, has stoically maintained that it has the authority, under a variety of acts of Congress, to apportion all or part of appropriated funds as it sees fit. The interest of the scientific community in the affair is that about $600 million of the impounded funds were earmarked for scientific projects.

Representative John Davis, the chairman of the House Science, Research and Development Subcommittee, last week stepped into the fray by introducing an authorization bill for the National Science Foundation which is designed both to increase the NSF's budget for 1974 and to give Congress more control over the way in which it is spent. Specifically, Davis's bill breaks the foundation's budget down into a number of items and stipulates that if any money is withheld from the total budget for the foundation, it must be taken from each item on a *pro rata* basis. Such a requirement would prevent a repetition this year of the familiar pattern, in which Davis's committee votes to increase the NSF's budget for education and graduate student support, only to have the Office of Management and Budget withhold that specific increase and effectively wipe out Congress's attempt to stamp its own priorities on the budget. Davis's proposed formula would, of course, leave congressionally determined priorities intact, even though funding for each item might be reduced.

In other developments related to the power of the purse, a special subcommittee of the Senate on the Separation of Powers provided a forum for several shouting matches between senators and members of the Administration, but produced little of substance. Congress also decided to opt for a head-on clash with President Nixon over his impoundments by directing him to spend all of the $225 million he has withheld this year from the Rural Environmental Assistant Program. All indications are that Nixon will veto the bill, and since it was passed in the House of Representatives by 251 votes to 142, it will need to pick up more support to get the two-thirds majority needed to override the veto.

A more promising development was the publication of an interim report by a special joint committee set up last year to devise a plan for Congress to set its own budget ceiling. The committee has suggested that bipartisan units should be established in both houses of Congress, with representation from appropriations and taxation committees. The idea would be for the committees to draw up spending ceilings and revenue raising targets early in the sessions, and that the appropriations committees would work to them. The machinery for implementing such a proposal will take several weeks to work out, however, so next year's budget will have to be set in the usual manner.

ENERGY POLICY

AEC to the Fore

by our Washington Correspondent

The Federation of American Scientists has suggested that the Atomic Energy Commission should broaden the base of its activities and become the chief agency in the federal government concerned with energy policies. The commission already has the authority for certain non-nuclear operations, the federation says, and "it is self-evidently the strongest of the government agencies for this purpose". The idea would be to transfer to the AEC energy-related programmes of other federal agencies, to turn the Atomic Energy Commission into an Energy Agency. The FAS has felt moved to recommend such a reorganization because the so-called energy crisis is so acute that it cannot wait for longer-term bureaucratic solutions.

President Nixon's reorganization plans call for a Department of Natural Resources to be established by amalgamating several existing agencies, including those having responsibility for energy production, but the FAS points out that the plan has been languishing in the committee rooms of Capitol Hill for two years, and stands little chance of being speedily accepted this year. Broadening the activities of the AEC would, however, not require massive government reorganization.

Part of the plan would also be to divorce the AEC's regulatory responsibilities from its promotional responsibilities by setting up a single energy regulatory agency with responsibility for controlling nuclear energy, gas, oil and coal.

The plan is, however, unlikely to find friends in the White House, because President Nixon is expected soon to propose again the creation of a Department of Natural Resources.

NEWS AND VIEWS

Continuing Classification of Research

THE article on page 449 by Dr F. Winterberg is interesting in itself but it is also the tip of a large, awesome and unnecessary iceberg. What Dr Winterberg does is to calculate the possible usefulness of small fission explosions, induced with the help of a powerful beam of laser light, as a means of triggering off thermonuclear explosions in a surrounding envelope consisting of a mixture of deuterium and tritium. His article includes, in passing, an expression for the critical mass of a quantity of fissionable material—an unusual occurrence in the published literature but an expression which is now thoroughly familiar among physicists in ordinary conversation. The object of the exercise is to demonstrate that it may be more efficient to bring about small releases of thermonuclear energy by using a microfission explosion as an intermediary than to attempt to use a laser pulse to compress a thermonuclear mixture directly with the help of a laser beam. In a sense, the fissile material, because of its high density, can act as an amplifier of the laser pulse, releasing a pulse of neutrons which can directly play a part in the thermonuclear process. Nobody can tell, of course, from Dr Winterberg's account, whether his calculations would be borne out in practice. Engineers are quite properly fond of pointing out that a simple calculation like this is bound to be hypothetical in some degree. But everybody will agree that calculations like these are at once interesting and stimulating and there is much to be said for making sure that they are published.

This is why it is disturbing that in the past few months, there has grown up a cloud of officially inspired reticence about publication in the field in which Dr Winterberg works. It is widely known that the use of lasers as a means of stimulating nuclear explosions, fission or fusion, has in the past few years been considered seriously by the United States Atomic Energy Commission and similar organizations elsewhere. That is as it should be. But the US Atomic Energy Commission is also exceedingly sensitive about the publication of results in this intriguing field and, to the extent that practical applications may be concerned, that too is proper. The trouble is that the passion for secrecy which is properly applicable to the potentially practical applications of these new technologies is, of course, entirely inappropriate where theoretical considerations are concerned, especially when their authors have no official connexion with the Atomic Energy Commission. This is why it is a considerable scandal that there have recently been difficulties in refereeing articles submitted in good faith to journals, especially where the publications are American.

A glaring offence against seemly practice is described in *Physical Review Letters* (**30**, 1 ; 1973) by an editor of that distinguished journal, Professor S. A. Goudsmit. By that account, an article on laser-induced fusion was submitted to the journal and sent in the normal way to a knowledgeable referee. In due course, there emerged a referee's report which must surely take the prize for the most unhelpful document of this kind—the referee by all accounts explained that all but two short paragraphs of his report could not be transmitted to the editors of the journal until they had been declassified. The author guesses that the classified parts of the referee's report refer to those parts of his own article which had to be omitted because they dealt with classified material.

This tale is not merely a description of a nonsense but a serious criticism of the way in which professional scientists conduct themselves. Is it really credible that serious professional people should write a scholarly opinion on a colleague's work and send this to the security men, not to the person for whom it is intended? Is it sensible, in any case, that the US Atomic Energy Commission should persist with a policy on classification which fails to distinguish between the kind of work where secrecy is legitimately applicable—where imminent practical applications are in question, for example—and the theoretical work or basic research typified by Dr Winterberg's article? To pursue a policy like this is to recreate the frenzy of the 1950s. And because, where laser-induced fusion is concerned, the Atomic Energy Commission has apparently been trying to prevent independent authors from publishing their entirely independent research, is it not time that the scientific community said what it thinks of policies like these?

Relativistic Forms

IN both quasars and pulsars some parts of a system almost certainly have speeds relative to other parts that are comparable with the speed of light, c. If so, then some parts have speeds of this order relative to any observer. Thus it becomes of practical significance to discuss the consequences of such motions for the observable features of a system.

As an academic exercise, many authors have considered the subject, and there exist frequently quoted papers, in particular by Penrose, by Terrell, and by Weisskopf; also there is a good account of certain aspects in a recent textbook by Meyer-Arendt (*Introduction to Classical and Modern Optics*, Prentice Hall, 1972). But now that the subject has gained more than academic interest, a new critical review by Mathews and Lakshmanan (*Nuovo Cim.*, **12B**, 168; 1972) is specially timely, even though these authors mention topical applications only in passing.

Consider an observer O, in an inertial frame S, observing some given object K fixed in another inertial frame $\bar{S}$ which has uniform speed V relative to S, where V is comparable with c. If the applicability of special relativity is assumed, then what O sees at any instant is determined by "relativistic" effects and by the different times taken by light to reach O from various parts of K.

Several familiar assertions, that presumably originated as rough shorthand descriptions of valid results, are false as they are often presented.

- "Bodies are seen to undergo the FitzGerald-Lorentz (F–L) contraction." In fact, this contraction becomes evident only after the observations have been reduced by a standard procedure allowing, in particular, for effects of different travel times for light. As such effects are of first order in c^{-1}, whereas the F–L contraction is a second order effect, in general they produce much greater apparent distortion in the object as actually seen. In other words, classical effects outweigh relativistic effects in determining apparent visual forms.
- "Linear motion of an object produces apparent rotation." Although this is valid for a sufficiently small rigid rod, it does not correctly describe the appearance of other moving objects.
- "A moving rigid sphere always appears spherical." In fact a fast-moving sphere must in general appear distorted in a complicated fashion, although it happens to be true that it always shows a circular profile.

These and other qualitative features are well clarified in the paper by Mathews and Lakshmanan. Quantitatively, their discussion prompts the following treatment (although it is not explicitly presented by them), which makes it possible to deal graphically with all possible cases.

First, consider any particular plane Π in $S,\bar{S}$ that contains the direction of relative motion; in the usual way let $Oxy, \overline{Oxy}$ be rectangular frames in Π, fixed in $S,\bar{S}$, with axes $Ox, \overline{Ox}$ lying along each other and chosen so that $\bar{S}$ moves with speed V relative to S in the x direction. Write $\beta = V/c$, $\gamma = (1-\beta^2)^{-\frac{1}{2}}$. Let t be time in S, and let $O,\bar{O}$ pass through coincidence at $t=0$. Then a particle fixed in $\bar{S}$ at $P(\bar{x},\bar{y})$ has a history in S expressed by the Lorentz formulae

$$x - Vt = \gamma^{-1}\bar{x}, \quad y = \bar{y} \tag{1}$$

Consider the view at $t=0$ of the observer O stationed at the point O in S. He sees particle P at a point (x,y) of equations (1) such that a photon from $P(x,y)$ reaches O at $t=0$. So P has $t = -r/c$, where $r = |\mathrm{OP}|$, whence, from equations (1), $x + Vr/c = \gamma^{-1}\bar{x}$. If $\bar{x}$ is given, that is if P in $\bar{S}$ lies on a line of constant $\bar{x}$, it then follows that $P(x,y)$ in S lies on the locus (in polar coordinates r,θ)

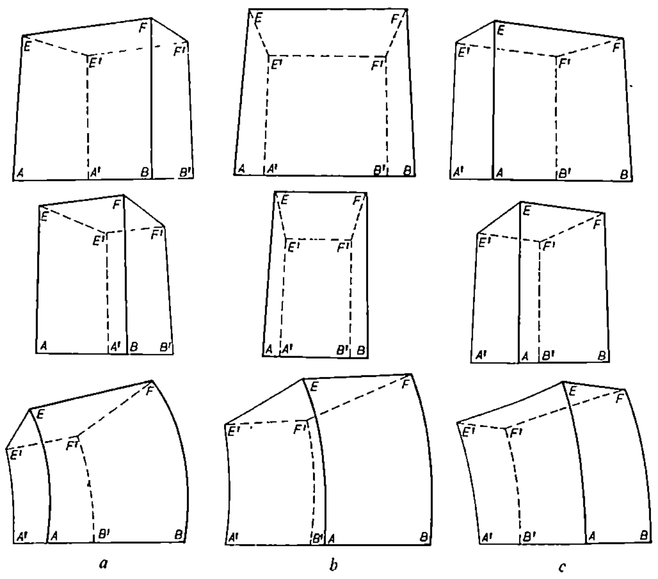
$$\begin{aligned} l/r &= \beta^{-1}\cos\vartheta + 1 \qquad \text{where } l = \beta^{-1}\gamma^{-1}\bar{x}\ (\bar{x}>0) \\ \text{or } l/r &= -\beta^{-1}\cos\vartheta - 1 \qquad \text{where } l = -\beta^{-1}\gamma^{-1}\bar{x}\ (\bar{x}<0) \end{aligned} \tag{2}$$

This is the set of branches convex towards the positive x direction of the family of similar hyperbolas having focus O, eccentricity β^{-1}, and vertices $(\bar{x}((1-\beta)/(1+\beta))^{\frac{1}{2}},0)$ for $\bar{x}>0$, $(\bar{x}((1+\beta)/(1-\beta))^{\frac{1}{2}},0)$ for $\bar{x}<0$. In S the lines of given $\bar{y}$ are $y=\bar{y}$. Thus the rectangular graticule in $\bar{S}$ is seen instantaneously from O in S as the mesh of hyperbolic branches (2), together with the lines of constant y. Thence the form of any given figure in the plane Π in $\bar{S}$ can be plotted in S as it is seen by O.

In particular, a rectangle in $\bar{S}$ with edges parallel to the axes is seen as having suffered contraction or expansion, combined with non-uniform shear, in the direction of motion. The apparent form of objects remote from the observer can, however, be obtained in general by using the asymptotes of the hyperbolic branches, instead of the curves themselves, and to this approximation the shear is, in general, uniform. This shows, as a special case, why a rod, at a large distance, appears to be rotated by the motion.

Similar results hold good in any other plane through Ox. So for three space dimensions the mesh can be completed by circles with axis Ox.

The procedure determines, in fact, the region in S that appears to be occupied by the object K when O views it at a particular instant. In order to describe precisely how O sees it, one ought then to apply the usual rules of perspective to the region. Mathews and Lakshmanan illustrate this in the case of a cubical box moving with one set of edges parallel to Ox with the results shown in their diagram, which is reproduced here.



The bottom row shows perspective drawings of the visual shapes of a moving cube ($\beta = 0.8$) as seen: *a*, while approaching, the apparent position being at about 30° to the y axis; *b*, when the apparent position is closest to the observer; and *c*, while receding, at about 30° to the y axis. If the cube itself or its Lorentz contracted form were held stationary at the above apparent positions, it would appear as depicted in the top or middle row respectively. The objects in *a* and *c* would be further from the observer than in *b* and so should seem smaller in overall size, but this is compensated by choice of scale in drawing. Note the progressively decreasing length of the near face (indicated by thick lines) as the cube moves past, and the fact that in *a*, even while the object is approaching, it is the rear face which is seen because of the apparent shear (and not the front face as in the case of the stationary objects). Reproduced from the paper by Mathews and Lakshmanan quoted in the text.

Finally, consider again the particle P in (1) with $\bar{x}=0$, $\bar{y}=0$. At his time T, say, O sees P at position $x = Vt$ where $T - t = x/c$ which gives $x = VT\,(1+V/c)^{-1}$. Thus $\mathrm{d}x/\mathrm{d}T = V(1+V/c)^{-1}$. Now suppose that $V(=-W)$ is negative, then $-\mathrm{d}x/\mathrm{d}T = W(1-W/c)^{-1}$. This is greater than W, for all $W>0$, but it is also greater than c if $W > \frac{1}{2}c$. In this last case O may say he sees P approaching him in such a way that the distance to P seems to be decreasing at a speed greater than the speed of light. This is essentially the example of the phenomenon given by Mathews and Lakshmanan. It shows in an almost trivial way how an apparently natural measure of speed evaluated from observations might happen to give a value greater than c. It has also been suggested that the interpretation given to some observations of quasar phenomena may be a slightly more sophisticated instance of the same general type of occurrence. So long as the situation is understood, there is nothing "wrong" with it.

W. H. McC.

Infection in Pregnancy and Foetal Growth

INFECTION during pregnancy is well recognized as a significant cause of foetal loss and morbidity. Abortion, congenital anomalies, retardation of foetal growth, and leukaemia have been ascribed to a wide variety of organisms with varying degrees of suspicion or proof. The infections recognized as causing retardation of human foetal growth include rubella, cytomegalic inclusion disease and, less commonly, toxoplasmosis. Although the mother may show little evidence of illness the infective agents of these conditions all cross the placenta readily and infect the foetal tissues, particularly in the first half of pregnancy. Involvement of the developing central nervous system is frequent and may result in mental retardation, hydrocephalus or microcephaly. Bacterial infection can cause equally severe illness or death in the neonate, but bacterial infections in the mother have not been shown to cause retardation of foetal growth. In asymptomatic maternal bacilluria the babies tend to be of low birth weight as a result of premature onset of labour rather than failure of foetal growth (Wren, *Med. J. Aust.*, **2**, 596; 1969).

R. L. Naeye has investigated the cellular basis of retardation of foetal growth seen in rubella and cytomegalic inclusion disease and has found that the basic defect is a deficiency in the cell populations of many of the organs throughout the body (Naeye and Blanc, *J. Amer. Med. Assoc.*, **194**, 1277; 1965; Naeye, *Amer. J. Clin. Path.*, **47**, 738; 1967). Confirmation that failure of growth may be a direct result of virus infection comes from the tissue culture work of Rawls and Melnick (*J. Exper. Med.*, **123**, 795; 1966) who have shown that the doubling time for fibroblasts is prolonged from the normal of 24 hours up to 48 or 72 hours in cultures infected with rubella virus.

On page 460 of this issue of *Nature*, C. R. Coid and D. B. Ramsden, of the Clinical Research Centre, Harrow, report experiments on mice which show that an inapparent maternal infection with Coxsackie B3 virus on day 8 of pregnancy causes retardation of foetal growth. The ratio of serum albumin to α_1 foetoprotein was higher in the newborn mice which were growth retarded than in control mice of the same gestational age although they matched those of immature control foetuses; this suggests an impairment in development of the plasma proteins. Further work on this model will clearly be needed to establish whether the viral infection causes retardation of foetal growth by an indirect effect, such as depression of maternal appetite, or through a direct action on the foetus such as that shown for rubella.

Although the enteroviruses have not been implicated as causing retardation of growth of the human foetus they are coming under increasing suspicion as causative agents for congenital anomalies. A large prospective study carried out by G. C. Brown at Ann Arbor has shown that inapparent maternal infections with Coxsackie viruses are significantly associated with a variety of congenital anomalies, particularly those affecting the heart. Sixty-five of 117 mothers giving birth to infants with cardiac anomalies had Coxsackie infections in pregnancy as compared with 68 of 219 controls. Most of the significant differences between the groups was accounted for by infections with Coxsackie B3 and B4 viruses (Brown, *Arch. Environ. Health*, **21**, 362; 1970). Indeed from the data of this survey it should be possible to confirm or refute the importance of maternal viral infection (or at least infection with enteroviruses, adenoviruses or influenza viruses) as a cause of retardation of human foetal growth. Conversely the experimental model produced by Coid and Ramsden could be useful for confirming the teratogenic potential of the Coxsackie viruses suggested by epidemiological surveys.

Additional support for a possible role of chronic infection in the causation of some cases of retardation of foetal growth is given by the finding of high levels of serum IgM in twelve of twenty-eight growth retarded infants (Yeung and Hobbs, *Lancet*, i, 1167; 1968).

Further work on the experimental aspects of viral infection in pregnancy may well show that a significant proportion of perinatal loss and morbidity is associated with inapparent viral infections in the mother.

J. S. W.

VIROLOGY

Pox in Monkeys

from our Medical Virology Correspondent

ALL nonhuman primates, as well as other animals, have a viral flora indigenous for that species and, although crossing of the species barrier undoubtedly occurs, it is not known to what extent this happens in nature. Seroepidemiological data collected thus far do not support the hypothesis that a reservoir for smallpox exists in wild monkeys and apes, but natural poxvirus infections of nonhuman primates do occur.

Monkeypox virus was first identified in 1958 (P. von Magnus *et al.*, *Acta Pathol. Microbiol. Scand.*, **46**, 156; 1959) during an outbreak of a vesicular eruptive disease among captive nonhuman primates in Copenhagen. The pustular disease was similar in distribution to variola in man and it was recognized as a poxvirus by its morphological appearance in the electron microscope and by its serological relationship to vaccinia. The first six cases of human infection with monkeypox were identified 12 years later in West Africa. There was a prodromal illness of a few days' duration followed by a vesiculopustular rash which was peripheral in distribution. All six patients recovered, although three were severely ill. Monkeypox virus was isolated from four patients and serological tests were positive in all six patients. Two of the patients had occasionally eaten newly killed monkeys and others had played with the viscera of monkeys. Spread of the infection from person to person had not occurred and no evidence of infection was observed in households where patients with monkeypox lived.

In 1971, another virus (Chimp 9) was isolated from the kidneys of a chimpanzee which was illegally shot in the Republic of Zaire in an area where human cases of monkeypox had occurred (S. S. Marennikova and colleagues, *Bull. Wld Hlth Org.*, **46**, 599; 1972). This virus was identical with the three "wild white" poxviruses isolated by R. Gispen of Utrecht in 1967 from the kidneys of apparently healthy *Cynomolgus* monkeys and these behaved more like smallpox than monkeypox. It is obviously essential that the extent of the relationship between all these virus strains be clearly established and a start in this direction has been made.

Marennikova and colleagues (*Arch. Ges. Virusforch.*, **33**, 201; 1971) compared the morphology of five isolates of simianpox virus and found that four out of the five viruses formed a homologous group differing in some respects from other poxviruses. The other strain of virus, which was isolated from apparently healthy monkey kidney, was indistinguishable from variola virus. Rondle and Sayeed (*Bull. Wld Hlth Org.*, **46**, 577; 1972) studied the growth characteristics and serological reactions of three monkeypox virus strains and found that monkeypox strains constitute a homogeneous poxvirus entity but that they can be differentiated from other poxviruses and that serologically they are more closely related to variola than to vaccinia or cowpox viruses.

To date thirteen confirmed cases of monkeypox in man have been reported from Liberia, Sierra Leone, Nigeria, Zaire and the Ivory Coast and some possible implications should be considered. Is there in West Africa a smallpox-like disease in animals which can spread to human populations? It is of interest to note that a fatal pox disease in *Mycetes* and *Cebus* monkeys in remote Brazilian forests was reported by Blayer as long ago as 1922 (*Münch. Med. Wschr.*, **69**, 1009), yet an intriguing observation is that in spite of extensive field surveys monkeypox in monkeys seems to be rare in West Africa and even serological surveys have yielded poor results. Yet a corollary to the first question is what is the possibility of epidemics arising in man once the present primary protection against smallpox has waned? Many ecological factors are undoubtedly involved in the distribution of viruses and these have not been clearly defined; but the need for the continuation of smallpox surveillance programmes is paramount.

FOSSIL RECORD

Palaeontology Moves On

from a Correspondent

For the meeting of the Palaeontological Association at Oxford on December 18–20, the council invited talks on all aspects of the subject, which has evolved considerably in the past decade.

Six contributors were concerned with the origins of higher taxa; Dr J. W. Valentine (University of California, Davis) outlined more theoretical aspects of phyletic interrelationships, and Dr R. P. S. Jefferies (British Museum (Natural History)) discussed the origin of the chordates on the basis of the early Phanerozoic fossil record. Other speakers based conclusions directly on fossil evidence, and in particular reflected the impact of scanning electron microscopic studies on skeletal microarchitecture and its phylogenetic significance.

The role of the palaeontologist in the interpretation of ancient environments received attention from several speakers, as did problems of functional morphology and palaeoecology of extinct organisms. All speakers in these categories revealed the extent to which palaeontologists have moved into the fields of ecology, and showed how ecological studies on living organisms are becoming an important factor in both the teaching of, and research in, the subject. Dr J. H. Lipps (University of California, Davis) reviewed work on adaptive strategies of Recent Foraminferida with its obvious consequences in the understanding of the palaeoecology of the group, and R. M. Kier (Smithsonian Museum, Washington) showed spectacular time lapse films of living echinoids which revealed many functional aspects; this work should prove valuable in assessing the nature of comparable features in related extinct forms.

Studies on regional faunal distributions and their role in the interpretation of ancient geographics received attention. Dr J. Murray (University of Bristol) outlined a Tertiary reconstruction of Western Europe based on comparisons with Recent foraminiferal assemblages, and Dr M. Hart (Plymouth Polytechnic), who drew his evidence from land-based samples and also JOIDES cores, demonstrated the value of regional microfaunal studies in understanding the early history of the Atlantic.

HAEMOGLOBIN

Intermediates in View

from our Molecular Biology Correspondent

New essays in fitting mathematical models to haemoglobin oxygenation curves tend nowadays to provoke in the outsider, depending on temperament, either mounting hysteria or a contented indifference. Even to the interested, the dispiriting suspicion that one has been here before is hard to fight down. But this is deceptive, for much progress has been made, and in particular Perutz's model for the oxygenation mechanism, which seems to follow almost irresistibly from the structural differences between the oxygenated and unliganded forms, has placed something of an obligation on physical chemists to see how equilibrium and kinetic properties in solution fit into this quite explicit framework. An important step in this direction was made by Ogata and McConnell (*Biochemistry*, **11**, 4792; 1972) who, while adhering to the principles of a fully concerted mechanism as the basis of co-

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States of Myosin

The contraction of muscle involves a displacement of myosin cross-bridges between the thick and thin filaments. When ATP is absent the bridges are in contact with the actin filaments, while making an angle of about 45° with the myosin filament axis. In the presence of ATP, on the other hand, they lie perpendicular to the thick filaments. The movement of the bridges between these states is presumed to lead to displacement of the thick and thin filaments relative to each other.

Analysis of myosin ATPase kinetics has shown that the rate-limiting step is the dissociation of the products, ADP and phosphate, from the active sites. The dissociation of the actin-myosin complex by the ATP is rapid. Thus when ATP is present one observes only the state in which the myosin is complexed with the hydrolysis products. An article by Mannherz *et al.* in next Wednesday's *Nature New Biology* (February 21) deals with the situation brought about by use of an ATP analogue, α,β-methylene-ATP, which differs from ATP in that the release of the hydrolytic products is rapid. Thus in the presence of this form the predominant structural state will be the one in which the active sites carry substrate rather than product.

The results show that the actomyosin complex in this system is unstable, myosin being dissociated from F-actin in the ultracentrifuge. In muscle fibres this effect is reflected by complete relaxation on addition of the analogue. Furthermore, the characteristic 145 Å reflexion in the X-ray pattern of insect flight muscle containing ATP vanishes when the ATP is replaced by the analogue. Because the 145 Å reflexion is associated with the perpendicular position of the cross-bridges, and its absence is also a characteristic of muscles in rigor, it follows that the bridges either enter their angled configuration, or possibly are in some way randomized.

These results support the view that the ATP complex is associated with a different structure from that of the ADP complex, and that the ATP is normally hydrolysed on the back-stroke of the bridges before they return to their perpendicular orientation. This sequence is also required by the kinetic rates, which indicate that the enzymatic activity resides in myosin uncomplexed with actin.

operativity—that is to say a two-state conformational equilibrium, involving low and high-affinity (R and T) forms —have expanded the model by permitting differences between the intrinsic oxygen affinities of the α and β-chain haems. The further assumption that there is no cooperativity between the ligand binding steps in either state, so long as there is no transition from one to the other, forbids any sequential component in the mechanism.

The choice of numerical parameters to test the model against experimental data is never, of course, wholly self-evident, and admits of a certain degree of sophistry. Ogata and McConnell base their choice of oxygen dissociation constants for the α and β chains in the R state on values reported for single chains (concerning which, it must be conceded, there has been some argument). Those for the T state they draw from their own measurements on hybrids, in which either the α or the β chains are in the cyanmet-form, and therefore functionally silent. The only other parameter of the model is the allosteric constant, L, which governs the position of the equilibrium between the T and R conformational states, with all haems unliganded. The effective value of L is modified by the presence of the cofactor, diphosphoglycerate, or of an analogue, because this binds to the T state only and so shifts the equilibrium in its favour by a factor that depends on the cofactor concentration and its (known) binding constant.

Ogata and McConnell use a spin-labelled cofactor analogue, the paramagnetic resonance spectrum of which is sensitive to its precise environment, and indicates that the two hybrid species, with the α and β chains respectively in the cyanmet-form, are conformationally indistinguishable, at least by this criterion. With the aid of a value for the parameter L, which is set at 3,000, the system at any given cofactor concentration can be completely described in terms of the balance of T and R forms, and the degree of saturation of the α and β chains in either state. At any given level of oxygen saturation, it turns out that the fractions of molecules in the R state are always highly, and those in the T state slightly, saturated, that is to say that the unliganded and fully liganded forms predominate in accordance with the observed cooperativity. In the absence of cofactor, the $T\rightarrow R$ transition occurs largely when the total ligand saturation is about half, whereas in its presence, most of the transition ensues only when three oxygen molecules have been bound. This agrees with indications from several experimental lines. Saturation curves of two abnormal haemoglobins, one an α, the other a β-chain variant, can be fitted if the binding constants in the T states of the abnormal chain, and in particular the values of L, are grossly changed, so as to make the R form accessible in all binding states.

Another β-chain variant, haemoglobin Kansas, where the replacement occurs at the $\alpha_1\beta_2$ subunit interface, and so might well be expected to affect the relative energies of the two conformational states, shows the same kind of anomaly in reverse by two very direct criteria. Hopfield, Ogawa and Shulman (*Biochem. Biophys. Res. Commun.*, **49**, 1480 ; 1972) have found that the rate constant for carbon monoxide uptake is independent of the degree of saturation, whereas in normal haemoglobin there is an increase in rate, in consequence of the appearance of the rapidly reacting R form, at a saturation corresponding to nearly three ligand molecules bound. Moreover, Ogawa, Mayer and Shulman (*ibid.*, 1485) find that oxyhaemoglobin and carboxyhaemoglobin Kansas are pulled into the R form by diphosphoglycerate or its analogues, as reflected by the appearance of features in positions of the proton magnetic resonance spectrum uniquely associated with the deoxygenated condition of the normal protein. This means that, even when oxygenated, the T state is energetically sufficiently accessible to be populated with the aid of the additional stabilization conferred by cofactor binding.

Supporting the many lines of evidence that now point to higher oxygen affinity of the α compared with β chains in the T state are experiments of Huestis and Raftery (*ibid.*, 1358), who have introduced a trifluoroacetyl group on cys-93 of the β chain. The ^{19}F NMR spectrum emanating from this group is very sensitive to events involving the β chain. Comparison of the oxygenation-induced shift with spectrophotometric measurements of total oxygen uptake confirms that oxygenation must start at the α chains. Two minuscule dimples in the ^{19}F NMR spectrum at intermediate stages of oxygenation are interpreted in terms of signifi-

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B Cells Responsive to Phytohaemagglutinin

NOT so long ago the thought that lymphocytes could actively proliferate was far from the minds of pathologists and haematologists. When Nowell concluded in 1960 that phytohaemagglutinin (PHA), a protein extracted from seeds of *Phaseolus vulgaris*, caused active mitosis of human peripheral blood lymphocytes *in vitro* there was much amazement. Cytogeneticists were the first to take advantage of the result in order to display human chromosomes. Slowly immunologists came to realize that their favourite cell could perform an interesting trick *in vitro*. Concomitant with this realization came the knowledge that lymphocytes were heterogeneous in relation to their anatomical origins. In 1968 several investigators, working largely with mice, concluded that cells of thymic origin (T cells), rather than those derived from the bursa or its equivalent in mammals, were the PHA-responsive cells.

With great alacrity this finding was extrapolated to the human species and it was found that in immunodeficiency disease syndromes, which were supposed to involve T-cell insufficiency, PHA-responsive lymphocytes were few and far between. The advantages of having an *in vitro* measure of T cells in man were enormous and there seemed little reason to suppose that what had been proven beyond doubt in the mouse did not also apply to man. In next Wednesday's *Nature New Biology* (February 21) Phillips and Roitt present evidence which could prick this bubble of enthusiasm. Specifically the authors suggest that both B and T cells can respond to PHA in man in quite conventional cultural conditions.

Phillips and Roitt first found that approximately 30 per cent of blast cells in PHA cultures of peripheral blood lymphocytes stain with a fluorescent anti-light chain antiserum. This result suggested either that T cells develop immunoglobulin (Ig) on their surfaces when responding to PHA or that B cells, which are widely thought to have immunoglobulin on their surfaces, could be included among the responsive cells.

When tonsillar lymphocytes were run down columns coated with anti-Ig, the resulting T cell-rich population was transformed with PHA *in vitro*, but as few as 5 per cent of staining cells could be counted. By using dextranase it was possible to recover the retained B cells from the column coated with anti-Ig and these gave rise to 86 per cent staining blasts when cultured with PHA. Incidentally no controls are quoted in which dextranase was used to treat T cells to see if they then developed immunoglobulin on their surfaces. But aside from this peccadillo the evidence of Phillips and Roitt strongly suggests that B cells in man can transform to PHA and that PHA transformation is thus an unreliable criterion of T-cell numbers in the human species.

It seems that care must be taken in attributing any characteristic as an absolute marker of either T or B cells and that extrapolation between species in relation to the distinguishing features of the two cells is hazardous. It should be noted that this argument applies to the use of surface immunoglobulin as a criterion of the B cell.

cant concentrations of partially oxygenated species, which are inferred to be in some wise different from the pure T and R states. Taken at face value this would seem to add a new degree of complexity in the system.

This is perhaps a good moment to relate that my account some time ago (*Nature*, **237**, 481; 1972) of the work of Perutz and his colleagues on the structural and functional properties of ferrous-ferric hybrid haemoglobins occasioned a frightful eruption, and a rain of shrapnel. An irate reader wrote to state that Perutz had made a rudimentary error in his assignments of high and low-spin spectroscopic features in the visible, and had in other respects abused his data, and I was charged with perpetuating if not amplifying his errors. Having taken it all on the chin, I will not tax readers with the details: the model as outlined is now hanging fire, while Perutz prepares new arguments, which are promised in detail soon.

POPULATION CYCLES

Why Study Dispersal?

from a Correspondent

POPULATION cycles of abundance of small rodents have kindled interest in ecologists for almost half a century, and several theories purporting to explain them have been put forward. All these theories have been rather less than convincing because they lacked reinforcement from experiments in the field. Some interesting observations on rodent cycles are now put forward by Krebs, Gaines, Keller, Myers and Tamarin (*Science*, **179**, 35; 1973).

Krebs *et al.* started with the ideas put forward by D. Chitty (*Proc. Ecol. Soc. Aust.*, **2**, 51; 1967) that the genetic composition of the population changes during a cycle in numbers and that internecine strife is the factor ultimately responsible for population decrease. During a five-year period (1965 to 1970) Krebs and his colleagues studied the anatomy of field vole populations (*Microtus pennsylvanicus* and *M. ochrogaster*) in southern Indiana. The mechanics of the decline were obvious —a reduction in survival of early juveniles and in birth rate, but more important an increased mortality among the older animals. This increased mortality affected males and females differently at different times of the year. That mortality acts selectively in this way is thought to demonstrate that extrinsic factors are not the chief forces in population decline.

In order to investigate the intrinsic quality of population decline, Krebs *et al.* built a *Microtus*-proof enclosure and compared population increase within the fence with a control area outside it. The number of animals in both groups increased sharply but became excessively high only within the enclosure. It seemed that prevention of dispersal was largely the root cause. In the adjacent control area, the percentage losses of voles as a result of dispersal were much higher during population increase than during peak densities of population decline.

Using the genes *Tf* (transferrin) and *LAP* (leucine aminopeptidase) as markers, the authors found at these two loci large changes in gene frequencies which could be related to dynamic change in population number. During the increase phase, 89 per cent of the losses of heterozygous females (Tf^c/Tf^e—*c* and *e* are alleles of the *Tf* gene) from the control populations were caused by dispersal. This suggests that demographic events are genetically selective and dispersal losses are not equal over all genotypes. This is the first time a genotype for dispersal has been demonstrated in a natural population.

The hypotheses of population regulation by social stress have to explain the finding of *Microtus* populations in the enclosures at densities many times higher than normal without "stress" taking an obvious toll. Prevention of dispersal changes the quality of the enclosed populations compared with that of the controls. In spite of the high density they continue to breed, but the behavioural effects of crowding do not seem to cause voles to die. Only when starvation takes effect by decreasing survival and reproduction does the rate of increase start to drop off. However productive they may be, fencing experiments turn up many new questions. For example, does the differential dispersal rate of animals during the increase phase of the cycle cause the quality of voles remaining at peak densities in the wild to be different from the quality observed at far higher densities in enclosures?

Several experiments are suggested by Krebs *et al.* to examine the components and influences of dispersal. The first is to attempt to cause abnormal densities in other rodent species by preventing dispersal. Second, one-way doors fitted to fenced enclosures should allow population regulation through dispersal to occur. Third, because dispersal is relatively unimportant once peak density has been achieved, closing the doors at this time should have no effect on normal decline. Krebs *et al.* themselves state that they do not know whether the genetic changes they describe are causally related to population changes, or are just side effects of other changes.

The ideas reported here naturally refer to existent populations of voles. Dispersers from increasing populations colonize unoccupied areas and, because of the increased incidence of heterozygotes among their number, will establish populations rich in *Tf* heterozygotes. This does not seem to bestow any observable ecological fitness at this stage in the demographic pattern. Evidence from island studies indicates that isolated rodent populations are much like land-locked populations in their demographic development. In the light of the new observations it is these populations founded by colonizers from other populations, and in which dispersal is largely prevented, that should now be closely scrutinized.

Cyclic AMP and Chloramphenicol Acetyl Transferase

THE antibiotic inactivating enzyme chloramphenicol acetyl transferase is one of the numerous enzymes in *Escherichia coli* the synthesis of which seems to be regulated by cyclic AMP, but unlike the inducible enzymes involved in the metabolism of sugars, which are also regulated by cyclic AMP, chloramphenicol acetyl transferase is made constitutively. How cyclic AMP regulates the synthesis of chloramphenicol acetyl transferase is the question which de Crombrugghe, Paston, Shaw and Rosner have been investigating. As they report in *Nature New Biology* next week (February 21) it seems that both cyclic AMP and the nucleoside tetraphosphate ppGpp independently stimulate the synthesis of this enzyme.

The group used an ingenious and very sensitive assay for chloramphenicol acetyl transferase and found that cyclic AMP stimulates its synthesis about twofold. This indicates that the synthesis of this enzyme is not as strictly controlled by cyclic AMP as is the synthesis of β-galactosidase. To investigate the control mechanism further, de Crombrugghe *et al.* set up a cell-free system which synthesizes chloramphenicol acetyl transferase and responds to cyclic AMP which then stimulates a fifteenfold increase in the synthesis of this enzyme. This stimulation is specific, but ppGpp in the absence of cyclic AMP also enhances synthesis of the enzyme. By contrast, ppGpp alone does not stimulate synthesis of enzymes of the *lac* operon and other inducible enzymes. In short, the synthesis of chloramphenicol acetyl transferase is enhanced by cyclic AMP and ppGpp alone, whereas synthesis of other *E. coli* enzymes by ppGpp depends on the presence of cyclic AMP.

These differences justify further experiments aimed at elucidating in detail the mechanism of regulation of synthesis of this antibiotic inactivating enzyme.

ENZYMES

RNase H Activity

from our Cell Biology Correspondent

When an enzyme becomes as fashionable as reverse transcriptase from RNA tumour viruses has become since its discovery in 1970 one can guarantee that any interesting new claim about its properties will rapidly be confirmed or refuted, as the case may be. That is perhaps the chief benefit stemming from such competitive situations. Take, for example, the seminal observation reported by Mölling and her colleagues in 1971 (*Nature New Biology*, **234**, 240). They found that reverse transcriptase isolated from virions of avian myeloblastosis virus (AMV) has an associated ribonuclease H activity which specifically digests the RNA moiety of an RNA.DNA hybrid molecule but which does not digest single stranded RNA or double stranded RNA or DNA. This report stimulated several groups to pursue further the characterization of this RNase H activity, and during the past couple of months the fruits of their labours have appeared in print.

Baltimore and Smoler (*J. Biol. Chem.*, **247**, 7282 ; 1972) have reported that the DNA polymerase and RNase H activities of reverse transcriptase from AMV cannot be separated by analytical chromatography or centrifugation. And by using tailor made synthetic RNA.DNA substrates they established that the RNase H activity releases oligonucleotides and mononucleotides with 3′ hydroxy groups and 5′ phosphoryl groups. Because some of the products of digestion are oligonucleotides they describe this activity as an endonuclease.

Keller and Crouch (*Proc. US Nat. Acad. Sci.*, **69**, 3360 ; 1972), who also found that the DNA polymerase and RNase H activities of reverse transcriptase cannot be separated, studied the degradation of both synthetic RNA.DNA molecules and the RNA containing DNA of the plasmid *Col* E_1. Like Baltimore and Smoler they find that the products of digestion are oligonucleotides as well as mononucleotides, but their data also indicate that the RNase H activity requires a substrate, the RNA moiety of which has free ends. This would indicate that the viral RNase H activity is an exonuclease but it digests internal phosphodiester bonds presumably by leapfrogging from the free end to some internal position in the RNA chain. Whether such an enzyme should be called an endonuclease or an exonuclease is almost an argument over semantics. Keller and Crouch also established that the RNase H activity of AMV particles is distinct from the RNase H activity in chick cells and KB cells, an important point when it comes to deciding the origin of the enzyme.

Grandgenet, Gerard and Green (*J. Virol.*, **10**, 1136 ; 1972) have, by screening ten different viral reverse transcriptases, established that an RNase H activity is a universal property of reverse transcriptases from RNA tumour viruses. They have also shown that enzymes from different viruses have slightly different specificities for synthetic substrates, for example only the reverse transcriptases from Moloney mouse sarcoma leukaemia viruses and RD feline leukaemia viruses hydrolyse the poly(U) of poly(U).poly(dA).

A more interesting observation reported by this group (*Proc. US Nat. Acad. Sci.*, **70**, 230 ; 1973) is that the reverse transcriptase of AMV occurs in two separable forms : one consists of two polypeptide chains, an α chain with a molecular weight of about 65,000 and a β chain with a molecular weight of about 105,000 ; the other form is a single polypeptide chain with a molecular weight of 65,000. The two forms of the enzyme have antigenic determinants in common, the same template specificity and both RNase H and DNA polymerase activities. Reverse transcriptase from viruses other than avian RNA tumour viruses resembles the second form of the AMV enzyme, and consists of a single polypeptide chain. These data coupled with those of Keller and Crouch, and the properties of various mutants of avian RNA tumour viruses, strongly suggest that the α chain is coded by the viral genome. But what is the origin and function of the β chain? Perhaps this is the beginning of a story that will prove to be as complex as that of the origin and mechanism of action of phage Qβ RNA replicase.

The question of the role of the RNase H activity of viral reverse transcriptases is, of course, a matter of considerable speculation. This activity may well be necessary for the synthesis of a double stranded DNA provirus from a single stranded RNA viral genome. But that remains to be proven.

BIOLOGICAL CONTROL

Attack on Thistles

from our Plant Ecology Correspondent

In spite of the publicity which has been evoked by the successful biological control of certain species of pest, these success stories are still few in number. This is especially true of the control of plant pests by the introduction or encouragement of herbivore populations. Classic examples are the control of *Opuntia inermis* in Australia by the beetle *Cactoblastis cactorum*, and that of *Hypericum perforatum* in the rangelands of North America by the beetle *Chrysolina quadrigemina*.

It may seem strange that in northwest Europe, one of the most intensively farmed areas in the world, there are no examples of effective control of a weed species by introducing a predator. This is not because the area is lacking

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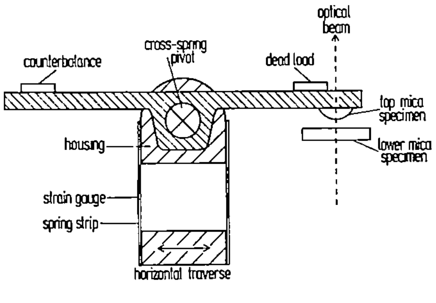
Shear Properties of Molecular Films

An investigation of shear in molecular films, which has a bearing on the boundary lubricating action of long chain amphipathic molecules (those with one end hydrophilic and the other end hydrophobic), is described by Israelachvili and Tabor in next Monday's *Nature Physical Science* (February 19). Previous related experiments have been carried out by Bailey and Courtney Pratt (*Proc. Roy. Soc.*, **A227**, 500 ; 1965) who studied calcium stearate films on curved mica sheets. These experiments used low pressures, and the sheets were flexible ; experiments using metal surfaces have also been carried out, but in these the area of molecular contact was not known precisely. In the experiments reported by Israelachvili and Tabor, both thickness and area of sheared film were measured and contact pressure could be varied from 10^5 to 10^7 N m^{-2}.



The experimental arrangement is shown in the figure. The mica sheets, with backs silvered, are glued to cylindrical glass supports and viewed by multiple-beam interferometry to determine the area of contact. The load applied (dead load) can be up to 50 g, and the sliding speed can be varied between 3 and 40 μm s^{-1}. Mono and multimolecular stearate films have been investigated. The results show that the first adsorbed monolayer is firmly attached to the mica substrate, and the shear strength (3 to 4×10^5 N m^{-2}) is much the same as that reported by Bailey and Courtney Pratt, and others. The thickness of the monolayer, 48 ± 3 Å, suggests that molecules stand normal to the mica surfaces. At contact pressures of up to 10^7 N m^{-2}, the limit possible with the present experiment, the molecules of the monolayer remain oriented normal to the surface of the mica; thicker molecular layers are, however, easily dislodged and broken up by the sliding process.

in weed species, nor is it attributable to lack of effort in attempting to find suitable biological control agents. For example, the creeping thistle (*Cirsium arvense*) is a troublesome weed of pastures in Britain and many other countries, both in Europe and North America. Following the work of Zwölfer on the insect predators of this weed, a chrysomelid beetle, *Haltica carduorum*, which is a native of southern Europe, was introduced into two British localities in 1969 (Claridge *et al., Entomologist*, **103**, 210 ; 1970).

The outcome of these introductions is now described by C. R. B. Baker, R. L. Blackman and M. F. Claridge (*J. Appl. Ecol.*, **9**, 819 ; 1972). Adult beetles imported from France were originally released in June 1969 at Silwood Park, Berkshire, and Llantwit Major, Glamorgan. They bred during the summer, but few survived the 1969–1970 winter. Those which did survive were first seen in mid-April, when the thistles had just begun regrowth after winter dormancy. Further introductions were made in summer 1970, but once again survival was poor.

Detailed studies of these populations showed that egg production was low and mortality was high at all stages in the life history of the beetle. Laboratory studies were carried out on the environmental requirements of the insect and it was found that there was a strong positive correlation between the rate of egg production by each female and temperature over the range 14° to 22° C. Egg mortality in the field was around 30 per cent when day temperatures were more than 20° C, but rose to 100 per cent if 15° C was not exceeded. Mortality among larvae was also high at low temperatures. Winter survival of adults was not studied in the laboratory.

The geographical distribution of *Haltica carduorum* in southern Europe coincides with situations where day temperatures in excess of 20° C can be expected regularly during the summer. Evidently the British climate is not so adverse that the completion of the life cycle is totally inhibited in this species, but it does seem to be detrimental to the maintenance of a viable population. Mean temperatures of 13° to 17° C, which were recorded in the field during these trials, are evidently sub-optimal for several stages in the life history of *Haltica*.

An effective biological control agent is one which is specific in its predation, which significantly reduces its prey population and which can maintain viable populations under the prevailing climatic conditions. Evidently *Haltica carduorum* fails on the third count; its effectiveness on the second count is also open to question. There are predators of *Cirsium arvense* with more northerly distributions and which are absent from Britain for reasons other than climatic ones, such as isolation by the post-glacial eustatic rise in sea level which has severed Britain from the Continent. The search for an efficient biological control agent of the creeping thistle must now centre upon these species.

GAS DISCHARGES

Computing Streamers

GALLIMBERTI reports in a recent issue of *Journal of Physics D* (**5**, 2179 ; 1972) that he has constructed a quantitatively successful model of the propagation of a streamer discharge in a gas which makes use of a simple energy balance criterion. In the past the predictions of streamer models have not been particularly accurate.

A streamer is a weakly ionized and slightly luminous channel which starts from the positive electrode and has at its tip a high concentration of positive charge. The streamer grows as shown in the diagram—photoelectrons produced in front of the tip by photons each generate their own small ionization avalanches by virtue of the local field around the streamer tip. In air at atmospheric pressure, for example, a field of more than 26 kV cm^{-1} is necessary for avalanche development to be viable.

Unfortunately the equations governing the development of a series of avalanches are, in practice, impossible to solve numerically; Gallimberti makes the simplifying assumption that the avalanches in front of the streamer tip can be represented by a single avalanche which starts immediately ahead of the streamer, somewhere along the line A but within the active region. The problem is then to calculate where the equivalent avalanche starts. Gallimberti uses as the basis of this calculation the energy balance equation

$$W_g + W_{pot} = W_l$$

where the parameters are respectively the gain of energy as a consequence of the applied field, the difference between the potential energies of the streamer tip and the sphere of positive ions created during the development of the equivalent avalanche, and the total loss of energy during the formation of the new avalanche.

During the computing process the lengthening of the streamer caused by each successive equivalent avalanche was reckoned to be twice the radius of

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Orbiting Systems, Mass Loss, and Gravity Pulses

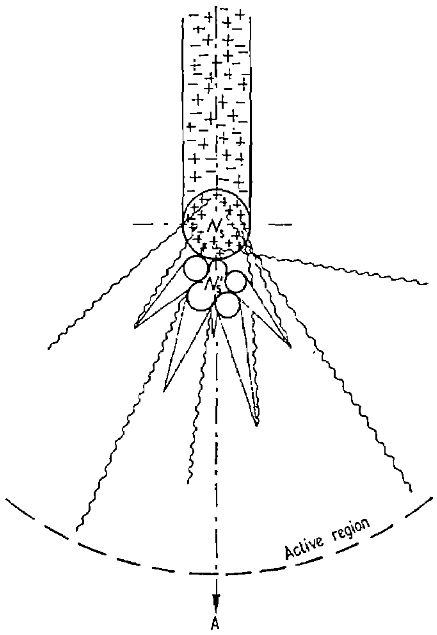
THEORETICAL physicists continue to be intrigued by the problem of how large quantities of gravitational radiation might be produced in plausible astronomical situations. In next Monday's *Nature Physical Science* (February 19), Jackson and Matzner describe the effects of sudden loss of mass from a primary object on a hypothetical small companion in orbit around the primary. Because the mass of the primary (M) changes abruptly, the secondary (mass m) experiences a changing acceleration. This "jerk", defined as the third time derivative of position, or rate of change of acceleration, can become very large for large M. Such a situation provides a powerful, if short lived, mechanism for the production of gravitational radiation, because the third derivative of the quadrupole moment of the pair m,M becomes large, and the rate of production of quadrupole gravitational radiation depends on the square of this derivative.

Some curious features emerge from the details of the analysis which Jackson and Matzner have made. If $\dot{M}$ is sufficiently large, the gravitational radiation shows similarities to radiation from a particle in a circular orbit; but in the case of the jerk mechanism information about the central gravity field—that is, about the nature of the mass M—is contained in the field equations. This seems to be a result of the requirement that the speed of light is constant; the information that M is changing must be transmitted throughout M, and this will take a different time for diffuse objects, compact stars, or black holes.

Could this jerk mechanism have a bearing on the seemingly large flux of gravitational radiation reported by Weber to be coming from the galactic centre? If the loss of mass occurs at the galactic centre, from a compressed object, and if the Sun is taken as the secondary particle, then the flux rate observed at the Earth should be only 10^{-7} times that claimed by Weber. "It is tempting," say Jackson and Matzner, "to attempt to sum the contributions of many particles m surrounding a central body undergoing mass loss." This would only help with the observational problem, however, if the jerk radiation originates at the small particles and in some sense in phase; then a reverberation could sweep the cloud of small particles as the information about the loss of mass from M spreads outwards.

Because the work described in next Monday's *Nature Physical Science* is based on the weak field approximation, the intriguing speculations encouraged by this last possibility should really hang fire until similar calculations have been carried out for strong fields. Jackson and Matzner promise that such calculations are now under way.

the tip of the avalanche. A streamer ceases to propagate, of course, when the local field in the vicinity of the tip of the streamer is no longer sufficient to allow further avalanches to form. Gallimberti's programs yield the length and velocity of the streamer, the current and charge in the external circuit, and the charge in the streamer tip, all as functions of time and for a given arrangement of electrodes.



The way in which a streamer grows. New ionization phenomena can only take place in the active region. (From *J. Phys. D.*, **5**, 2183 ; 1972.)

The accuracy of the calculations can be judged by a comparison between calculation and experiment for an electrode arrangement of a square rod separated from a plane by 150 cm. The applied voltage at the start of streamer formation was 125 kV in this case. It turned out that the computed and measured values for the total streamer lengths were 10.9 and 11.2 cm, and the initial velocities 0.23 and 0.28 cm ns^{-1}.

MICROTEKTITES

Bottle Green Variety

from our Geomagnetism Correspondent

TEKTITES, those strange natural glass bodies with diameters usually of several cm, are apparently limited to four large areas (strewnfields) and four corresponding ages. The Australasian, Ivory Coast, Czechoslovakian and North American strewnfields have approximate ages of 0.7, 1.0, 15.0 and 35.0 million yr, respectively—ages which in some cases are supported by more than one method of dating. The Australasian tektites, for example, have been dated by both K–Ar and fission track methods and are found in a layer coinciding with the Brunhes–Matuyama geomagnetic reversal boundary. Microtektites (diameters <1 mm) are also associated with the two most recent strewnfields, having been found in adjacent deep sea sediment cores. Most of these microtektites ("normal microtektites") are physically and chemically similar to the larger tektites, but a few (0 to 20 per cent in any given core) have significantly different properties. These are the so-called "bottle green microtektites"; and the fact that they differ from normal microtektites has led several workers, beginning with Martin (at the US Meteorological Society Conference in 1967), to suggest that they are igneous glasses rather than proper tektites.

Martin has been followed in this by several others; but Glass (*J. Geophys. Res.*, **77**, 7057 ; 1972) has now put paid to the whole idea by showing that although bottle green microtektites differ in some (but not all) respects from the normal variety they differ even more from igneous glasses. For one thing, a search of more than seventy deep sea cores from around the world has shown that bottle green microtektites are found only in cores which contain normal microtektites and, moreover, only in the particular sediment layers containing the normal bodies. On the other hand, the converse is not true—all normal microtektites are not associated with bottle green ones. Thus bottle green microtektites were found in both cores containing Ivory Coast microtektites but in only three of the thirteen corresponding Australasian cores. Even those cores containing normal microtektites but no bottle green microtektites, however, contain yellow-green varieties with physical and chemical properties intermediate between the two. In this sense, the bottle green–normal association is enhanced, and is made even stronger by the coincident ages (because of coincident layering).

Palaeomagnetism and *G. truncatulinoides*

IN next Monday's *Nature Physical Science* (February 19), Theyer shows how palaeomagnetism has been used to invalidate what was once one of palaeontology's most reliable datum planes. The plane in question is defined by the first appearance of the planktonic foraminifer *Globorotalia truncatulinoides* and was taken to mark the onset of the Pleistocene at about 1.8 million yr ago. But if this interpretation were correct, the appearance of *G. truncatulinoides* should lie within the Matuyama reversed geomagnetic polarity epoch, whereas Theyer finds that in the southern hemisphere, south of 36° S, it lies within the earlier Gauss normal epoch.

Theyer's evidence comes from twelve palaeomagnetically dated and six other deep-sea cores from south of Australia and the Tasman Basin. Because radiolarians are the most widely used biostratigraphic correlators with the geomagnetic polarity-time scale, Theyer has used them in conjunction with already available palaeomagnetic measurements to match the cores to the time scale. Having done this, he finds that in ten of the palaeomagnetically dated cores *G. truncatulinoides* either first appears close to the base of the Gauss epoch or is already present towards the end of the epoch. Moreover, it is not possible to attribute the presence of *G. truncatulinoides* in this time period simply to the effects of reworking or contamination, for the populations are strong and, in those cores deposited far enough north to have experienced climatic variations, the abundance of *G. truncatulinoides* fluctuates in phase. Correlations with other planktonic foraminifers also tell the same story.

One of the implications of the appearance of *G. truncatulinoides* some 1.0 to 1.5 million yr before its previously known appearance in lower latitudes is that the supposed evolution of *G. tosaensis* into *G. truncatulinoides* at the Pliocene–Pleistocene boundary cannot be correct. Theyer believes, therefore, that the two are subspecies or even ecological variants which appeared in different areas at roughly the same time. The evidence is that *G. tosaensis* is not found at all in cores from south of 36° S and that others have already reported the appearance of *G. tosaensis* at the base of the Mammoth polarity event in a tropical core.

To put it another way, the suggestion now is that *G. truncatulinoides* and *G. tosaensis* appeared more or less simultaneously, the former at latitudes higher than 36° S and the latter at lower latitudes but probably with a very slight overlap. The latitude separation, in turn, implies environmental (probably climatic) control on the evolution into the two subspecies.

Finally, Theyer's revision has an interesting general consequence. Because the appearance of *G. truncatulinoides* has been regarded as one of the most reliable Neogene foraminiferal datum planes, it has been used in numerous studies involving latitudes higher than 36° S. Presumably, therefore, if Theyer is right, the conclusions drawn in previous studies are wrong and also require revision.

This evidence, although strong, is circumstantial; but more direct support comes from comparisons of physical and chemical characteristics. The Australasian and Ivory Coast bottle green microtektites are very similar in appearance; they are transparent pale green and vary in shape from spherical to irregular. But by contrast with the range of smooth to grooved and pitted surfaces of the normal microtektites, the bottle green ones have deeply corroded surfaces. Thus the normal and bottle green microtektites are quite distinguishable from each other on the basis of surface texture and colour (although more easily in the case of the Australasian bodies). On the other hand, in both areas the normal and bottle green microtektites are similar in that they do not contain crystalline inclusions—and this distinguishes them from igneous glasses. Moreover, although the bottle green microtektites differ from the normal variety in having no vesicles, they also differ in this respect from igneous glasses. Finally on the physical side, bottle green microtektites are found to have higher densities and refractive indices than most normal microtektites; but the similarities are maintained in so far as the group of high-magnesium Australasian tektites reported by Chapman and Scheiber (*J. Geophys. Res.*, **74**, 6737; 1969) also have the higher densities. In short, the density ranges for normal and bottle green microtektites overlap.

As far as chemistry is concerned, the Australasian bottle green microtektites have significantly different compositions and trends from those of the normal microtektites. The two Ivory Coast types have different compositions—the bottle green ones have lower SiO_2, Na_2O and K_2O, but higher MgO, FeO and CaO—but the same oxide trends. Moreover, the bottle green microtektites from the two areas have similar compositions. The normal Ivory Coast microtektites are, however, in many ways similar in composition to high silica Australasian bottle green microtektites, the chief difference being the lower FeO and the higher CaO and TiO_2 of the latter. And the bottle green Australasian microtektites overlap in composition with the high magnesium tektites of Chapman and Scheiber.

All this is very confusing; but what it amounts to is that the normal and bottle green microtektites have both chemical differences and similarities. The fact is, however, that whatever the differences are, they are distinct from the differences between microtektites and igneous glasses. This is particularly apparent when compositions are plotted on an $MgO–K_2O–Na_2O$ ternary diagram. Both tektites and microtektites have higher MgO and lower Na_2O contents than igneous glasses for similar SiO_2 contents, and the bottle green microtektites lie on a trend which continues smoothly into the normal microtektites and tektites. The trend for igneous glasses is conspicuously different. Glass thus concludes that the bottle green microtektites are properly named.

But does this conclusion have any bearing on the origin of tektites and microtektites, a matter of long dispute? Glass believes it does. Whatever the precise origin of tektites, most workers seem to agree that they are produced in some sort of impact process—and if this is the case, tektite compositions should give some clue to the nature of the originating material. The most abundant bottle green microtektites have SiO_2 contents of 48 to 54 per cent and on average comprise 61 per cent pyroxene and 22 per cent plagioclase. They also contain normative corundum and quartz and small quantities of orthoclase and ilmenite. These data suggest that if the originating material were igneous it would have been gabbroic. It would seem, however, that the Al_2O_3 and MgO contents of the bottle green microtektites are much higher than in gabbroic rocks. Furthermore, the bottle green microtektite compositions are not similar to that of any important meteorite group nor to any produced by the mixing of normal meteoritic material with normal tektite material. Nor (*pace* certain theorists who would place the origin of tektites on the Moon) do they correspond to any important group of lunar material returned to Earth. The obvious conclusion is that if the originating material is on the Earth it must be extremely rare—so rare, in fact, that none has yet been found. The constraint in the origin of tektites and microtektites is thus severe.

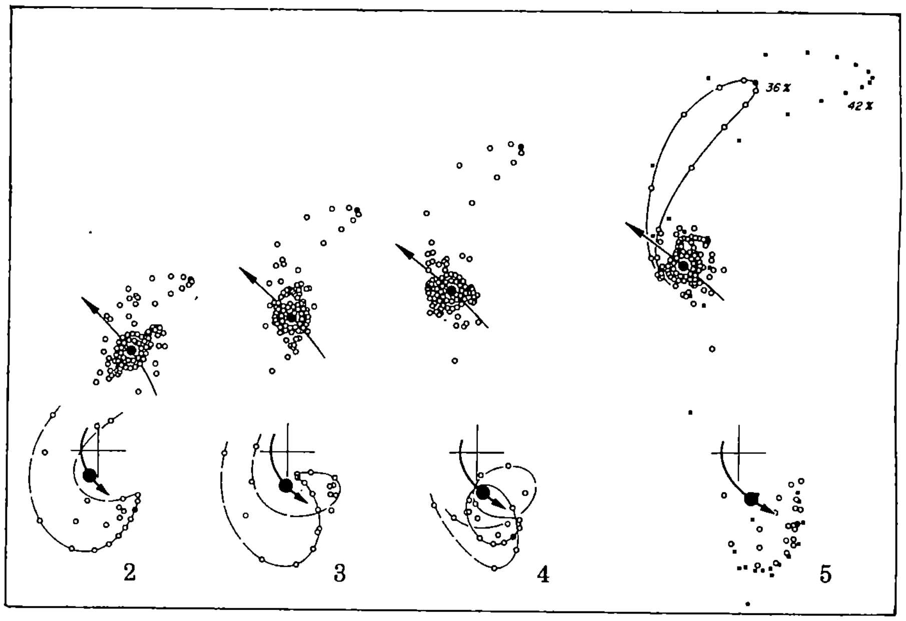
COSMOGENY

Origin of Bridges and Tails in Galaxies

by our Cosmology Correspondent

THE bridges and tails seen in some galaxies may simply be tidal relics of close encounters, according to Toomre and Toomre (*Astrophys. J.*, **178**, 623; 1972). They have studied such events in a "deliberately simple minded" computer simulation in which each encounter involves only two galaxies and is roughly parabolic, and in which each galaxy is idealized as a disk of noninteracting test particles initially orbiting a central mass point.

Two particularly interesting features emerge from the analysis. After a small companion passes such a galaxy, the primary disk may deform into an arm or a bridge extending towards the secondary, together with a counter arm on the opposite side. After a similar encounter with an equal or more massive partner there is a tail on the far side of the primary; on the near side there is an "avalanche" of particles which are mostly captured by the satellite galaxy (see diagram). Toomre and Toomre also offer specific models to account for the shapes of the interacting pairs Arp 295, M51+NGC 5195, NGC 4676 and NGC 4038/9.



The later stages of a "flat" parabolic passage of "companion" four times as massive as the "victim" galaxy. The companion carries off many particles from the victim, which grows a tail on the opposite side.

Copernicus Published as He Perished

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Nicholas Copernicus was born on February 19, 1473, yet his great work *Revolutions* was only published in March 1543, two months before he died.

THE scientific community all over the world this year will recall that our present conception of the Universe owes its origin to Nicholas Copernicus, who was born exactly half a millennium ago. Throughout the preceding millennium and a half the Earth had been contrasted with the heavenly bodies: they moved and it did not. This motionless Earth was stationed at the centre of a finite sphere, which rotated once a day, carrying with it the bright stars embedded in its otherwise invisible surface. Below this outermost limit of the Universe with its "flaming ramparts", the planets circled at various distances from the centrally located immobile Earth.

This hallowed picture of the cosmos was drastically rearranged by Copernicus. He was the first thinker to set forth cogent reasons for lifting the Earth up out of the centre of everything and putting it where it really belongs: a planet among its fellow planets.

In so doing, he defied common sense. For Earth the planet must move, unlike central Earth. Indeed, Copernicus conferred three motions on the Earth: its daily rotation around its own axis produced the unending succession of day and night; its annual revolution around the Sun caused the cyclical sequence of the four seasons; and a third movement explained the precession of the equinoxes. Yet if the Earth rushed and whirled through space at such awesome speed, it could be objected by common sense, why do its inhabitants not feel its powerful propulsion and ceaseless gyration?

Confronted by an unfamiliar idea, common sense might laugh derisively. But the reaction of entrenched ideology and established religion could be more sinister. A letter written by Copernicus to a clergyman expressed his fear of opposition from the peripatetics and theologians.

Recently we were told that Copernicus was timid, hardly the word to characterize a prudent man living in a harsh age wracked by political warfare and religious strife. When a play produced in a theatre not far from Copernicus's home ridiculed his idea of a moving Earth, he may have recalled with a shudder that Socrates was mocked on the Athenian stage before the popular jury sentenced him to a lethal dose of hemlock.

Some two decades earlier, in the first flush of creative joy at his discovery of the geokinetic astronomy, Copernicus had circulated among selected specialists a few handwritten copies of the brief preliminary draft of his new cosmology. Even then he discreetly withheld his name as author from his so-called *Commentariolus*.

Evidently Copernicus ardently desired to submit his ideas to the scrutiny of contemporaries. Yet he had no wish to become a martyr. Anonymity was one way out of his dilemma. But there was also another.

On November 1, 1536, a highly placed prelate of the Roman Catholic church wrote to Copernicus, urging him to communicate his still unpublished findings to scholars, and offering to have all of the astronomer's writings copied in his quarters at the cardinal's expense and sent to Rome. A stony silence was Copernicus's response.

By contrast, during the previous year Copernicus had received a visit from an old friend, who was now the secretary of the king of Poland. In this capacity he was in touch with important personages in Vienna, then the capital of the Holy Roman Empire and a pulsating hub of the publishing trade. There was no printing press in that "most remote corner of the Earth", as Copernicus himself described the place where he spent most of his time during the last three decades of his life. Hence the Vienna connexion offered him a golden opportunity.

One method of testing the soundness of an astronomical system is to compare its detailed predictions of what will be seen in the heavens with the observed phenomena as they occur. The logical outcome of a prolonged and extensive investigation, such as Copernicus conducted for nearly half a century, is the computation of a fresh set of astronomical tables. The forecasts derived by extrapolation from these new columns of figures could be critically juxtaposed, not only alongside future observations but also past tables, now submitted to competitive examination.

This was a test which Copernicus welcomed. "For the common advantage of everybody" he was then engaged in preparing an almanac which he was confident was far more accurate than the one in common use. But his busy visitor had to leave before Copernicus could finish his almanac. A copyist was hastily called in, who under these circumstances naturally made some mistakes. These had to be corrected and the gaps had to be filled by a qualified person in Vienna. The royal secretary's accompanying letter stated that Copernicus "for many years has believed that some motion must be granted to the Earth, and asserts that the motion of the

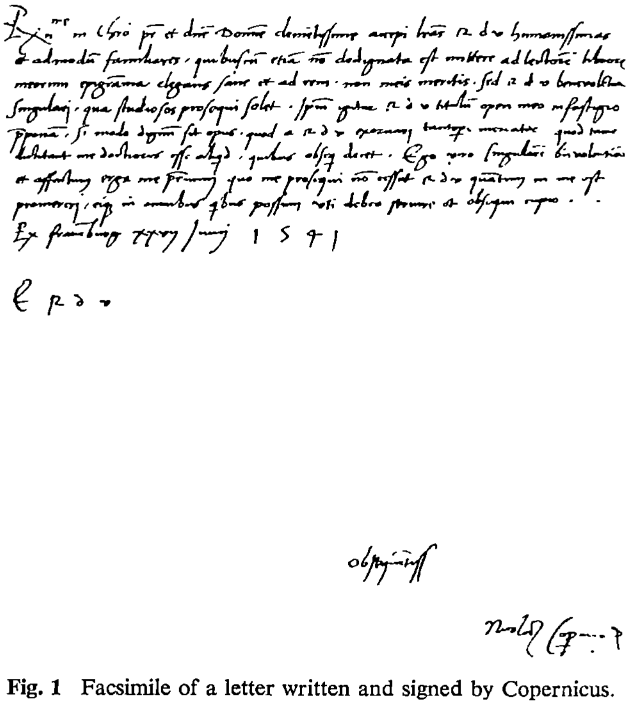

Fig. 1 Facsimile of a letter written and signed by Copernicus.

Earth is not felt". Perhaps this shock to common sense, perhaps the lacunae and errors, perhaps the death of the king's secretary, prevented the publication of Copernicus's almanac. It has disappeared without leaving a trace.

In deciding what should and what should not be made public, Copernicus followed the lead of the ancient Pythagoreans. Because he admired their code of conduct, his astronomical system was often identified with theirs, although the resemblances are slight and the differences significant. As a closely knit brotherhood, the Pythagoreans believed in "entrusting the secrets of philosophy only to faithful friends and associates, and not committing those secrets to books nor disclosing them to everybody". While making his almanac available for publication, Copernicus did not turn over the novel principles on which his new astronomical tables and almanac were based. By withholding his reasoning, which he realized was in conflict with traditional ideas and common sense, Copernicus felt that he would "provoke no dispute among philosophers".

His best friend disagreed, for he knew that current astronomical theory badly needed overhauling—and the ecclesiastical calendar was woefully out of joint. Aware of Copernicus's exceptional talent and unremitting labours, he kept on pressing for complete publication of the new system.

There were two works in the field which could serve as possible precedents. The Alfonsine Tables, prepared at the expense of and named in honour of a thirteenth century king of Castile, formed the model preferred by Copernicus. This mediaeval Spanish product reported no observations on which the Tables were based, and enunciated no rules or principles by the light of which they had been drawn up. In spite of their skeletal shape, they were entirely satisfactory to the practical astronomer (and astrologer), who had no particular interest in the underlying theory. By contrast there was Ptolemy, the greatest of the ancient Greek theoretical and practical astronomers. His *Syntaxis* (often miscalled the "Almagest") was crammed full of observations, theorems, proofs, deductions, and diagrams. His illustrious example was therefore to be shunned, in Copernicus's judgment. For how could acrimonious controversy be avoided if geokineticism were to be fully exposed to public view?

But Copernicus's friend could not be persuaded or silenced. He insisted on the difference between science and politics. In delicate negotiations undertaken to conclude a vexatious war or regulate troublesome public affairs, secrecy was justified as a temporary expedient. But once secluded discussions were successfully terminated, the dark curtain would be raised to disclose the new situation. On the other hand, if Copernicus behaved like a special plenipotentiary, hiding his principles and displaying only their results as a set of stark naked tables, who thereafter would ever be able to unravel the intricate details and lay bare the underlying conceptions? Would not the scientific community be forever deprived of the sorely needed light which Copernicus for purely prudential reasons was hiding under a bushel?

This seesaw dialogue might have batted the ball back and forth indecisively and interminably, had not a fresh player entered the stalemated game from the outside world. A young German professor of mathematics arrived on the scene, attracted by rumours of revolutionary innovations and eager to assess them at first hand for himself. Received with open arms and granted access to the concealed manuscript, within a brief span of time he became thoroughly convinced that the gossip he had heard in far-off Germany was no exaggeration. Here in Copernicus's closely reasoned and thoroughly documented presentation lay, like a restive foetus, the long-awaited reformation of astronomy.

Yet no amount of persuasion, however earnest or skilful, could induce Copernicus to release his own manuscript to the press. He raised no objection, on the other hand, to his disciple's swift composition of a *First Report* about the Copernican astronomy. This was rushed to a printer in the Hanseatic town of Gdańsk, where it was published in March 1540. Copies were dispatched at once to influential friends everywhere. Its author, recognizing that it "could be considered heretical (as the monks would say)", waited anxiously for the explosion that he anticipated. None occurred. Instead, a second edition of his *First Report* was issued at Basel in 1541. Still no detonation was heard.

At last Copernicus was convinced. He finally consented to the publication of his manuscript, preceded by a magnificent plea for freedom of thought and expression. In particular he besought the bibliolators to refrain from twisting Scripture to the detriment of science. Lactantius was no mean writer, but he made fun of those pagans who maintained that the Earth was round. The implication was clear. The theologian had his own important task, but unless he also had additional training that made him an expert in the mathematical sciences too, he was not qualified to sit in judgment on the new astronomy. That was written for specialists. This is the meaning of Copernicus's most famous utterance ("*Mathemata mathematicis scribuntur*"), which carries no overtones of condescension or contempt for the untutored, as has been mistakenly charged by his would-be detractors. After all, Copernicus wrote his *Revolutions* in Latin (as a century and a half later Newton, that greatest of Copernicans, did with his even more momentous *Principia*), and for the untutored anything in Latin was, of course, a closed book. When Copernicus decided to publish, he addressed himself to his compeers.

He laid no claim to originality. Far from professing to be the first thinker to have recognized the true cosmic status of the Earth as a planet in motion, he delved into whatever ancient writings happened to be available in a quest for his own precursors. From them he obtained, not his ideas, but a protective shield for his ideas. The point is that these were not really new. They were quite respectably old, but somehow they had become buried beneath the accumulated debris of the centuries, and merely had to be disinterred and cleaned up.

Not as a revolutionary, nor as a subversive, but as a resuscitator of forgotten wisdom, did Copernicus tardily appear in public. His youthful German collaborator made a fair copy of Copernicus's precious autograph (now splendidly reproduced in photofacsimile), and elicited from the Duke of Prussia requests addressed on September 1, 1541, to the Elector of Saxony and the University of Wittenberg for permission to publish Copernicus's *Revolutions*.

If it is true that science owes the publication of Newton's *Principia* to Edmond Halley, it is equally true, as George Joachim Rheticus later declared, "Had I not visited Copernicus, his work would absolutely not have been published".

It was Rheticus who made the arrangements with an active and prosperous shop in Nuremberg to print Copernicus's masterpiece. But Rheticus could not finish reading the proofs and doing the editing because he had to leave for the University of Leipzig, which had just appointed him professor of mathematics.

His place was taken by a local minister, whose hobby was the mathematical disciplines. His philosophy of science was diametrically opposed to Copernicus's, as he well knew from the letters they had already exchanged. Taking advantage of Copernicus's grave illness in remote Frombork and of his own inside position as editor, he surreptitiously introduced into the front matter of the *Revolutions* an unsigned foreword wholly foreign to Copernicus's intention. Whereas the astronomer firmly believed that he had disclosed an essential feature of the physical universe, his editor presented it as though it were merely a convenient device for making computations. It was not necessarily true, and might even be false.

Thus speciously accoutred, Copernicus's *Revolutions* came off the Nuremberg press in mid-March 1543. By the time a copy reached the author in distant Frombork, he was lying barely conscious on his sickbed. Copernicus never knew about the intrusive, well-intentioned, but misleading foreword, for, on May 24, 1543, he perished as he published.

Real Space Crystallography

J. W. STEEDS, G. J. TATLOCK
& J. HAMPSON

H. H. Wills Physics Laboratory, University of Bristol

We have discovered an image plane technique of crystallographic analysis which achieves spatial resolution of structural defects and diffraction information, reveals a lack of a centre of symmetry, requires only minute crystals and is rapidly executed.

IN spite of its achievements X-ray crystallography has a number of limitations. One is the loss of phase information in X-ray diffraction so that heavy atom derivatives of the crystal under investigation have to be obtained[1]; another is the limitation on crystal size which arises from the relatively weak interaction of X-rays with matter. If the crystals are too small, too imperfect or combined in a mixture of too many different components, X-ray methods break down; applications where problems have arisen are in the crystallography of biological molecules; martensitically transformed materials; polytypes of layer structures; plagioclase minerals, and the great variety of non-stoichiometric oxides. Electron diffraction which can in principle overcome these difficulties has until now generally involved too many mathematical problems to be useful[2], but recent developments in both experimental technique and interpretation indicate that electron microscope observations can easily yield the point groups of difficult crystal structures and make complete structure determinations possible.

Electron and X-ray diffraction are very different. Apart from the obvious differences in strength of interaction with a crystal and the resolution of the two techniques two other properties are important for the new approach. At 100 keV the electron wavelength is ~ 0.04 Å so that the Bragg angles are very small for electron diffraction. Moreover, owing to the existence of electron lenses observations can be made either in the image plane (for which there is strictly no X-ray equivalent although Lang topography is similar) or in the back focal plane of the objective lens (similar to the conventional X-ray diffraction pattern). If an aperture is introduced in the back focal plane to encircle either the direct or a diffracted path diffraction information may be recorded in the image plane. Because transmission specimens in the electron microscope have to be thin (~ 2000 Å) they bend very easily through angles large compared with the Bragg angle. The diffraction contrast in the specimen image is therefore in the form of lines joining parts of the crystal which diffract similarly (Fig. 1). To take a simple case, consider plane electron wave-fronts incident on a cylindrically bent crystal with a radius of curvature R. If there is appreciable diffraction when the waves are incident at the Bragg angle (θ_B) a dark line appears at that part of the crystal in a bright field (aperture encircling the direct beam) picture. At a distance $2R\theta_B$ away another line is formed by Bragg reflexion in the opposite sense. In some cases the region between the pair of contours is dark and this is due to the excitation of strongly absorbed lattice waves concentrated on the atomic planes[3] (contour C Fig. 1).

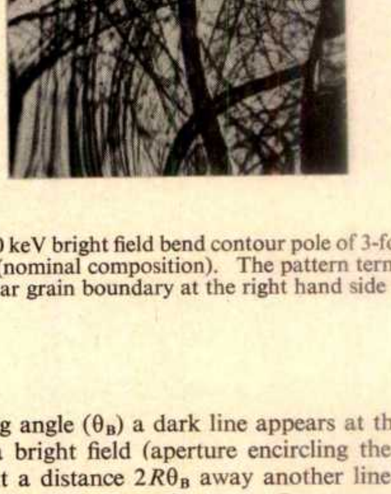

Fig. 1 100 keV bright field bend contour pole of 3-fold symmetry in Ta_2O_5 (nominal composition). The pattern terminates along the irregular grain boundary at the right hand side of the figure.

From this simple explanation it is clear that the specimen area shown in Fig. 1 is in the shape of a slightly distorted

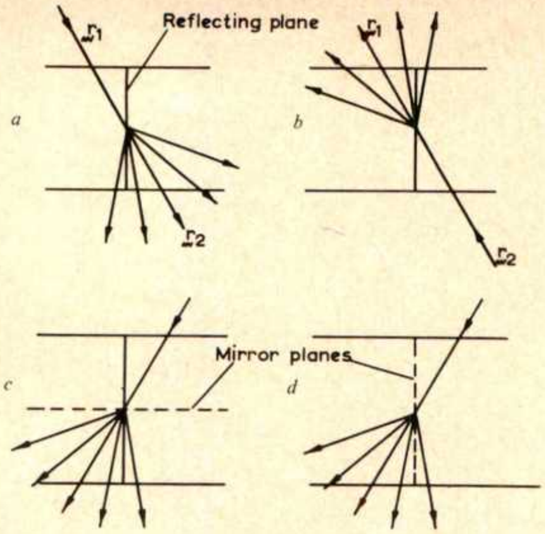

Fig. 2 Use of the reciprocity theorem together with crystal symmetry to deduce bend contour symmetries.

saucer over much of the field of view. As a result of the specimen geometry it is possible to tilt the specimen so that the electron illumination falls on it along any required direction within the range of the goniometer available. Commercially available electron microscopes may be equipped with goniometer stages permitting tilts of ±60° about any axis in the foil plane with specimen shift of only 1–2 μm.

Point Group Determination

The centres of various bend contour pairs in Fig. 1 are crystallographic zones. In practice therefore a prominent contour in the field of view is chosen and the specimen rotated and tilted until this zone intersects another prominent zone. The symmetry properties of this intersection, which is known as a zone axis pattern, are then examined. The pole in Fig. 1 may be seen to arise from an axis of three-fold symmetry with mirror planes every 60° and therefore the crystal is either trigonal or cubic. Subsequent rotation and tilt experiments reveal that the specimen has the point group 3*m*. Owing to high intensity of the electron beam and the ease with which the goniometry may be performed it is possible to arrive at the conclusion in the course of an experiment lasting about 30 minutes. Clearly *n* fold axes and mirror plates can be detected easily. What is more surprising is that it is also possible to tell from bright field micrographs whether the crystal has a centre of symmetry.

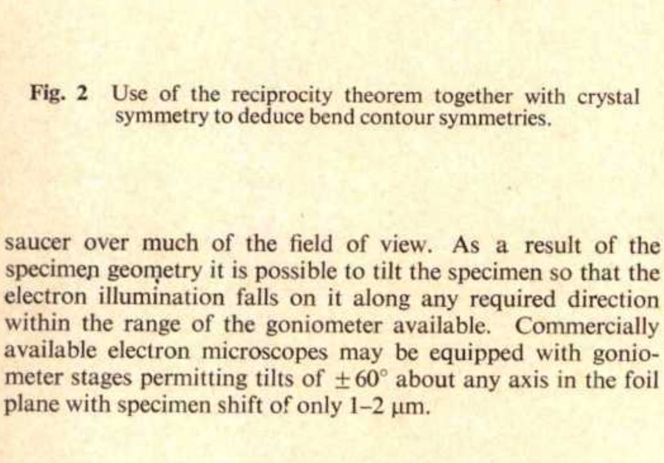

Fig. 3 Bright field bend contours at 100 keV on a polytype of molybdenite showing violation of Friedel's Law.

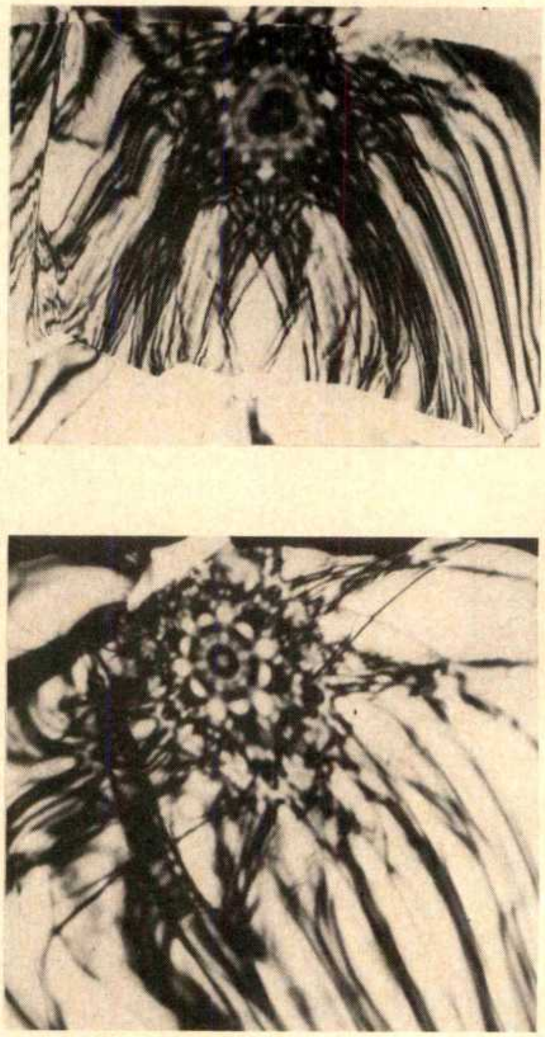

Fig. 4 Image detail in 3-fold and 6-fold zone axis patterns of different polytypes of MoS_2.

There has been misunderstanding over this point[4] and so we shall re-examine the argument which is based on the so-called reciprocity theorem. According to this theorem[5], if a signal is detected at a point $\mathbf{r}_2$ when a source is placed at another point $\mathbf{r}_1$, then the same signal in amplitude and phase would be detected at $\mathbf{r}_1$ if the source were placed at $\mathbf{r}_2$. In bright field the situations shown in Fig. 2 *a* and *b* are thus equivalent as are also *c* and *d* on addition of the mirror planes shown. By a minor adjustment of the argument we imagine the angle of incidence fixed and the foil bent. To a good approximation, therefore, we expect symmetric contours in bright field when *c* and *d* apply.

In the case of basal foils of a non-centred polytype (2T) of molybdenite, the mirror in Fig. 2 *c* is absent. $\{\bar{2}110\}$ planes have the mirror in Fig. 2 *d* and yield symmetric contrours (Fig. 3), but $\{1\bar{1}00\}$, lacking the extra mirror, give asymmetric contours (a violation of Friedel's Law). After tilting through the (0001) pole the asymmetry of the $\{\bar{1}100\}$ contours is reversed with respect to the $(\bar{2}110)$ contour, verifying the significance of this observation. Note that we have not made use of the projection or zero layer approximation which is often made in the theory of electron diffraction. Had we made this approximation the mirror plane of Fig. 2 *c* is added and hence symmetric contours would result in bright field. In molybdenite the large *c* spacing makes the effect of other layers of the reciprocal lattice particularly important.

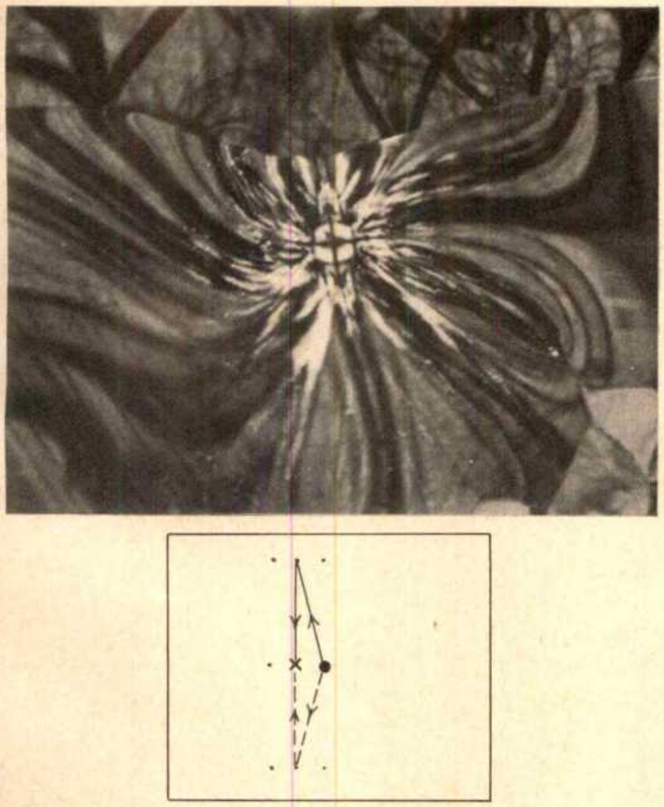

Fig. 5 Dark field electron micrograph obtained by encircling a forbidden spot occurring in a $(10\bar{1}0)$ pattern. The sketch shows a proposed pair of double diffraction paths.

Zone axis patterns shown in Fig. 4 easily discriminate between polytypes with three-fold and six-fold axes, a difficult problem by conventional techniques[6].

Because the area of interest is continuously in view while the specimen manipulation is performed, the diffraction information can always be obtained from this area, a considerable advantage over selected area diffraction techniques. Moreover, in view of the dynamic nature of the experiments two important benefits are obtained. First, the operator can test hypotheses about symmetry during the course of the experiment, by large tilts as well as by study of zone axis patterns. Second, imperfections in the diffracting area are much easier to detect as a series of diffracting conditions is carried past in quick succession than by a few static results which may in any event have been obtained under unfavourable conditions. There are two techniques in electron microscopy which are essentially similar to the one described here but differ in requiring flat specimens. These are the study of Kikuchi line patterns resulting from inelastic and thermally scattered electrons, and the convergent beam technique. The first is dependent on the presence of Kikuchi lines which are not at all common in imperfect crystals. Moreover, Kikuchi lines are invariably less detailed than bend contours and much harder to interpret. Convergent beam techniques as practised at present lack the resolution possible here and require special electron diffraction apparatus.

Space Group Determination

To take the next step in structure determination it is necessary to identify the forbidden reflexions. Owing to multiple scattering of electrons, which occurs even in very thin foils, diffraction spots can appear in forbidden positions. An experimental technique was devised for identifying this phenomenon during our work on Ta_2O_5. On rotating a foil about the *c* axis from $(11\bar{2}0)$ to $(10\bar{1}0)$ we found the spacing of spots in the *c* direction halved. Suspecting double diffraction, we used a very small objective aperture to encircle one of the two additional spots nearest the centre of the pattern. The resulting dark field micrograph is shown in Fig. 5. Strong diffraction is limited to the region of $[10\bar{1}0]$ zone axis, confirming the hypothesis. A possible diffraction path is indicated in the figure. Further information is visible in this result. The black cross at the centre of the pattern implies that the electron beam is incident either perpendicular to a screw axis of the crystal structure or parallel to a glide plane. Under these circumstances the possible routes to the forbidden positions may be arranged

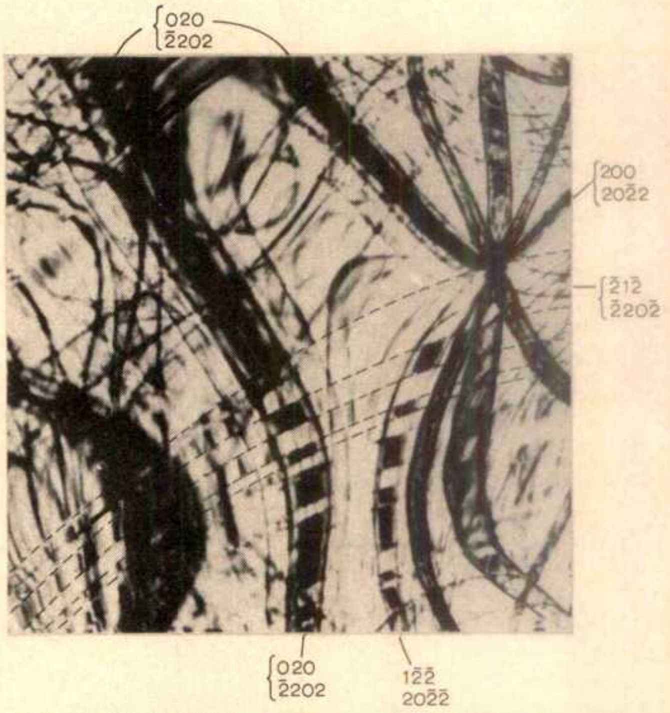

Fig. 6 Bright field bend contours at 100 keV in a multiply twinned Ta_2O_5 specimen. Changes in the form of the 020 contours are due to their transformation to $\bar{2}1\bar{2}$ in the twinned crystals.

in pairs contributing equal diffracted amplitudes of opposite sign[7]. The space group of the new form of Ta_2O_5 is found to be $R\bar{3}2/c$.

Minimum Crystal Size

The limitations on the nature of specimens which are suitable for the new method of analysis are not too severe. They concern the curvature and microstructure of the foils. If a foil only bends through a fraction of a Bragg angle in the field of view it would be too laborious a matter to piece together a contour map. In fact a misorientation of about 5° is a convenient working minimum. Flatter foils are generally suitable for Kikuchi line techniques. To make clear observations of symmetry it is necessary to work in relatively perfect regions and this imposes a limitation on the grain size of a polycrystalline material or the cell structure or dislocation density of a deformed material. It has been ascertained by experiment that a prominent contour is recognizable down to widths ~2000 Å so that a reasonable field of view in a suitable curved specimen can be as low as 0.5 µm for an equi-axial microstructure. This observation is compatible with the lateral coherence of the electron beam, about 100 Å. The limiting situation may be expected when a foil changes its orientation by 0.1 Bragg angle in this distance. Much better resolution is, however, possible in particular cases; an example is shown in Fig. 6. The trigonal phase ($\bar{3}m$) of Ta_2O_5 shown has been found by experiments in larger areas to contain twin boundaries. Many of the bend contours are unaffected by the twinning and run continuously from one phase to the next. An exception is the (002) contour that is notable for its dark centre. On passing into a twinned region the dark centre vanishes but the second line, and some of the other higher order lines, are continuous. Thus twins may be detected in regions less than 500 Å wide.

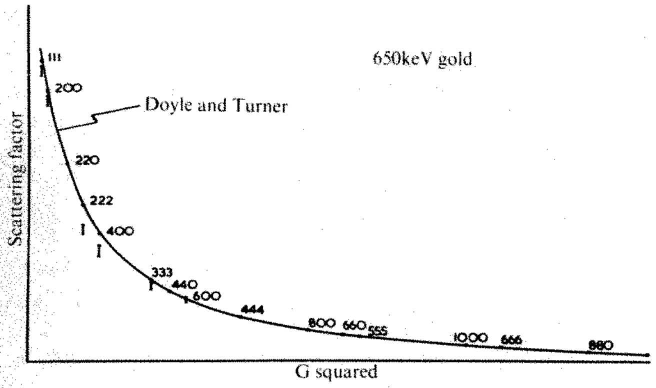

Fig. 7 Atomic scattering factor of gold deduced from bright field and dark field contours of 111 and 200 reflexions. The experimental results are indicated by error bars.

Atomic Arrangements

Our ultimate objective is to establish atomic arrangements in crystals of unknown structure. That there is a lot of information in micrographs such as Fig. 4 is obvious. Where the diffraction occurs from relatively close lattice planes the contours take the form of simple pairs of lines. In such cases, the theory of electron diffraction is not very different from that of X-ray diffraction and structure factors may be approximately determined from the visibility of the lines. This proposition has been tested in the case of mica, in the bend contour pattern. All strong lines are those which have large structure factors; none of the visible lines has a small structure factor. No doubt some reflexions with large structure factors do not give strong lines because of the combined effect of weak reflexions that are simultaneously excited. One effect of this type has been termed the critical voltage effect[8] and has been used to yield valuable information about the crystal potential[9].

More interesting are the contours corresponding to high voltages, high atomic numbers and large lattice periodicities, and to high symmetry zone axes. They are quite complicated in form and contain more detailed diffraction information. The first example of this sort to be thoroughly studied was the case of the (*nnn*) reflexions from gold at approximately 600 keV. The method of extracting information from the bend contours was based on the dispersion surface construction[10,11]. These are constant energy surfaces in reciprocal space equivalent to the Fermi surface for conduction electrons. Each point on a given surface corresponds to a particular direction of incidence, each surface to a Bloch wave in the crystal. The reciprocal of the separation of simultaneously excited points on the dispersion surface gives the depth periodicity in the crystal associated with energy transfer from one Bloch state to another. Thus it is possible to read out information from the bend contours about the dispersion surfaces and hence deduce the crystal potential. Results from the atomic scattering factor of gold are compared with the best available computed data in Fig. 7 (C. J. Richards, unpublished work).

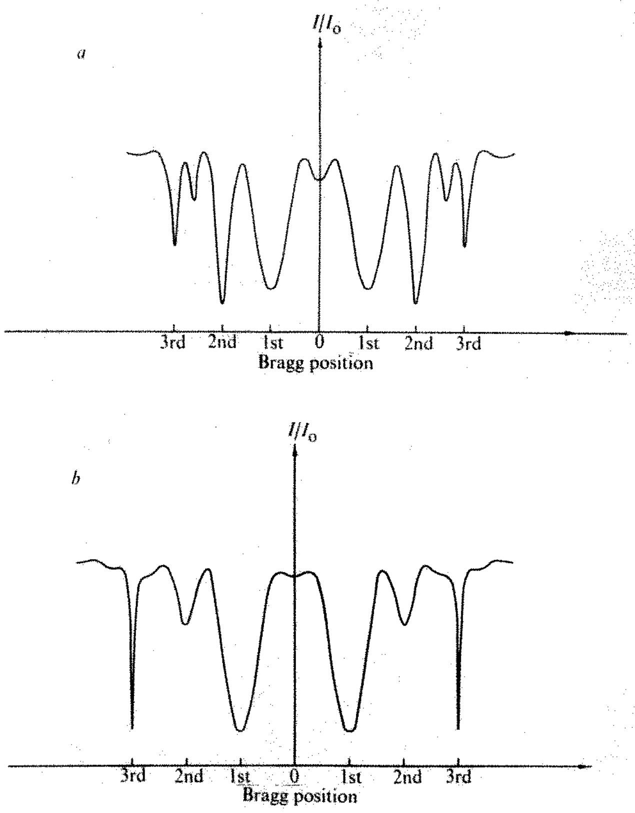

Fig. 8 Calculated contours for the $(10\bar{1}0)$ reflexion of (*a*) $2H_1$ and (*b*) $2H_2$ MoS_2 for a specimen thickness of 500 Å and an accelerating voltage of 100 keV.

More recently we have performed calculations for two hexagonal polytypes of molybdenite with the same space group but different atomic arrangement. The form of the $\{11\bar{2}0\}$ contours is essentially unchanged in the two cases and can be used to fix the foil thicknesses. The $\{10\bar{1}0\}$ and $\{\bar{1}103\}$ contours are quite different, however, and can be used to distinguish between the two atomic arrangements. The results of calculations for the $(10\bar{1}0)$ contour are shown in Fig. 8.

Where the diffraction problem is essentially one dimensional the many beam theory of Howie and Whelan has been used in calculations. However, the previously intractable problem of zone axis orientations has recently been solved by semiclassical methods[13,14], and the method of solution is not only quite straightforward but the process may be inverted to yield directly the atomic potential from experimental observations. We are now attempting a complete structure determination by the use of these recently evolved techniques.

The work reported here was carried out mainly in Bristol and also during a visit to the University of Santiago, Chile. We thank Drs M. V. Berry, A. Howie, J. A. Eades and P. A. Doyle for discussions.

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Tetrahydroisoquinoline Alkaloids: *in vivo* Metabolites of L-Dopa in Man

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Tetrahydroisoquinoline alkaloids have been unequivocally demonstrated *in vivo* for the first time in parkinsonian patients on L-dopa treatment. Their biosynthesis may have a profound bearing on how L-dopa acts.

ALTHOUGH the therapeutic effect of L-dopa in parkinsonism is no longer in doubt, its mode of action remains ill-understood. Early explanations in terms of simple replacement of deficient dopamine no longer seem wholly tenable. To account for all the observed clinical and biochemical phenomena, more sophisticated hypotheses have been postulated involving other pharmacologically active compounds derived from minor pathways of L-dopa metabolism (for review, see ref. 1). One such group of compounds, the tetrahydroisoquinolines, formed by the Pictet-Spengler condensation[2] of dopamine with an aldehyde, have been proposed by Sourkes[3] on theoretical grounds. Although many Schiff base derivatives of this type develop readily *in vitro* (for review, see ref. 4), evidence for their *in vivo* production in animal tissues is, at best, equivocal[5]. We report here the identification, in significant concentration, of two of the alkaloids, salsolinol and tetrahydropapaveroline, in the urine of patients with Parkinson's disease during oral L-dopa treatment.

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Analysis of Alkaloids

Much evidence (for review, see ref. 4) suggests that the formation of these compounds is facilitated by ethanol: salsolinol results from the reaction between dopamine and the ethanol metabolite, acetaldehyde; ethanol and acetaldehyde both appear to promote the synthesis of tetrahydropapaveroline which readily condenses *in vitro* from dopamine and the aldehyde deriving from the oxidative deamination of a second molecule of dopamine (Fig. 1).

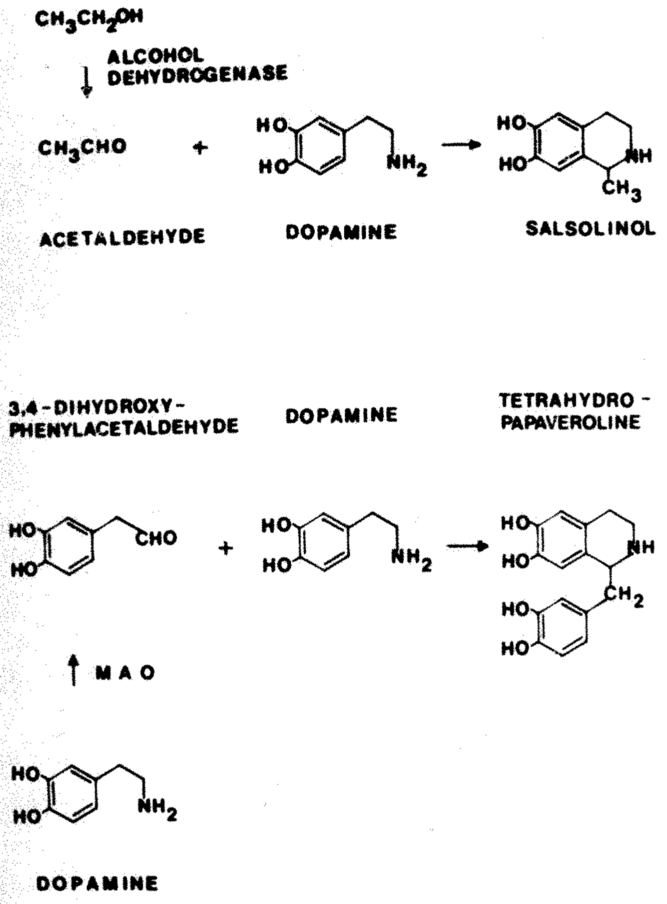

Fig. 1 Formation of salsolinol and tetrahydropapaveroline.

We used gas chromatographic methods to measure the concentration of these compounds in urine (ref. 6 and K. P. Wong, C. R. J. Ruthven and M. S., submitted for publication) from parkinsonian patients on L-dopa treatment before and immediately after ethanol ingestion. Four male patients (average age 56 years) who had responded well to an optimal oral daily dose of L-dopa (3–4 g) and understood the nature of the experiment, ingested either 75 ml. absolute alcohol (test), or 75 ml. water (control), made up to 160 ml. with water and flavouring at 0930 h over a 30 min period on two separate days. Urine samples were collected for the periods 0–3, 3–6, 6–9 and 9–12 h after the drink, acidified to *p*H 1–2 with hydrochloric acid and stored at −15° C until analysis.

Appreciable concentrations of salsolinol and tetrahydropapaveroline detected gas chromatographically as their pentafluoropropionyl (PFP) derivatives (Fig. 2) were excreted throughout the period under study (Fig. 3). We cannot, for a number of reasons, obtain any precise rate of synthesis from the serial 3 h excretion values from which the total 12 h output was calculated. These measurements, which varied widely, reflect the individual response of particular patients in whom dosage of L-dopa and its time of administration, gastric

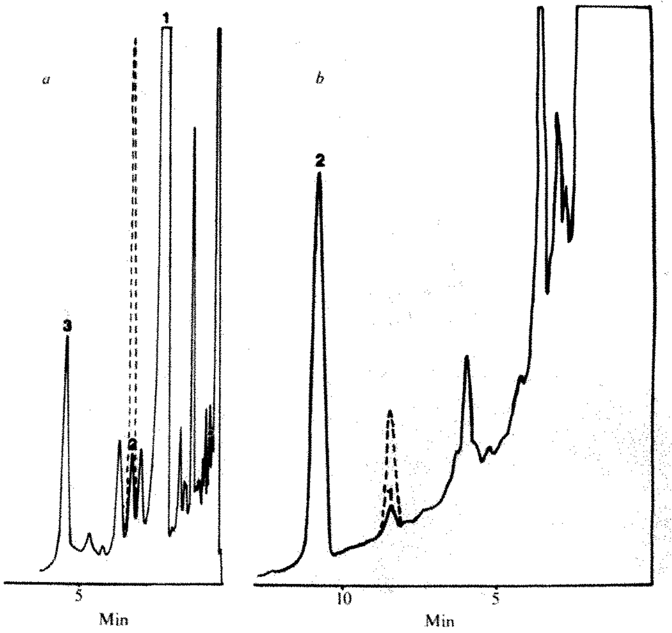

Fig. 2 *a*, Gas chromatogram of urinary extract containing salsolinol. 1=dopamine; 2=salsolinol (urinary output of salsolinol, ——); same urine sample after addition of internal standard, - - -); 3=γ-lindane. The concentration of salsolinol in this particular urine sample was approximately 300 ng/ml. and the amount injected approximately 60 pg. *b*, Chromatogram of urinary extract containing tetrahydropapaveroline. 1=tetrahydropapaveroline (urinary output of tetrahydropapaveroline, ——; the same urine sample after the addition of internal standard, - - -). The concentration of tetrahydropapaveroline in this particular urine sample was approximately 150 ng ml.$^{-1}$ and the amount injected approximately 750 pg. 2=dieldrin. Columns of acid-washed alumina$^{31-33}$ (0.5 g) were prepared from a slurry in 5 ml. sodium acetate reagent (0.2 M sodium acetate, 0.2% (w/v) EDTA, 0.1% (w/v) ascorbic acid, adjusted to *p*H 8.4 with 0.1 N sodium hydroxide). Duplicates (10 ml.) of each urine specimen were analysed by a method to be published in full elsewhere (K. P. W., C. R. J. R., and M. S.). To one of the duplicates had been added salsolinol (10 µg) (salsolinol hydrobromide purchased from Ralph N. Emanuel, Ltd., Wembley) and tetrahydropapaveroline (5 µg) as internal standards. Ascorbic acid (0.2 ml., 5% (w/v) freshly prepared) and EDTA (0.1 ml., 10% (w/v)) were added, in addition, to all duplicates^{34}, which were then adjusted to *p*H 8.4 and passed through the alumina column. After the column had been washed with sodium acetate reagent (5 ml.) and water (10 ml.), salsolinol and tetrahydropapaveroline were eluted with 0.5 M acetic acid (2.5 ml.) then water (2.5 ml.). Subsequent fractions, eluted with 0.5 M acetic acid, contained neither compound. A portion of the combined eluate (1 ml.) was taken to dryness and reconstituted in 0.2 ml. methanol/0.01 N HCl (1 : 1). One twentieth of this was used for analysis of salsolinol and one half for analysis of tetrahydropapaveroline. Pentafluoropropionyl (PFP) derivatives were prepared for gas liquid chromatography using pentafluoropropionic anhydride (ref. 6 and K. P. W., C. R. J. R., and M. S.). Immediately before injecting the samples, excess reagent was blown off under nitrogen and the derivatives reconstituted in dry ethyl acetate (0.1 ml.) containing reference standards of 1 µg ml.$^{-1}$ γ-lindane for salsolinol estimations and 2 µg ml.$^{-1}$ dieldrin for tetrahydropapaveroline. Recovery studies were carried out on PFP derivatives of salsolinol (100 ng) and tetrahydropapaveroline (500 ng). Samples were run on a 'Perkin-Elmer model 900' gas chromatograph with the following column conditions: carrier gas, nitrogen, flow rate 40 ml. min^{-1}; injection port temperature, 260° C; manifold temperature, 260° C; electron capture detector temperature, 300° C. A 12 foot glass column (i.d. 2 mm) packed with 10% SE54 on 'Gas Chrom Q', 80–100 mesh, was used at 210° C for salsolinol and 230° C for tetrahydropapaveroline estimations. Quantification was achieved by measuring peak heights and correcting for errors in injection using the reference standards. Salsolinol and tetrahydropapaveroline concentrations were calculated by comparison with the duplicate sample containing internal standards.

emptying and gastrointestinal absorption all differed. Also both compounds are labile in solution, so that standards must be freshly prepared in 0.01 N hydrochloric acid, and their PFP derivatives are unstable. They can be stored deep-frozen overnight in the presence of the pentafluoropropionic anhydride but, once dissolved in ethyl acetate for gas chromatography, are easily hydrolysed. Despite their lability in standard solution, however, they tend to be considerably more stable in urine. Fresh 3 h urine samples were therefore obtained from another four parkinsonian patients, two male and two female, on L-dopa (3–5 g day^{-1}), and analysed immediately. Although salsolinol excretion was somewhat higher, the data were not too dissimilar from those obtained in the previous experiment, indicating that deterioration during storage was at an acceptable level. Tetrahydropapaveroline was completely absent from a proportion of the stored specimens for reasons not yet determined. Another quantification difficulty was the wide recovery range (20–100%) of these compounds from different urine samples, for unknown reasons, and the values therefore must be considered only as semiquantitative estimates. We hope to obtain more exact information by the use of a reverse stable isotope dilution technique combined with gas chromatography –mass spectrometry[7].

Our data demonstrate the *in vivo* production of both salsolinol and tetrahydropapaveroline in man for the first time, and therefore, in order to establish their identity as precisely as possible, mass spectrometric studies were carried out. Standard spectra of salsolinol and tetrahydropapaveroline, as their fully substituted PFP and trimethylsilyl (TMS) derivatives, were recorded on both 'AEI MS12' and 'Varian-MAT 311' mass spectrometers by gas chromatographic inlet. The alkaloids were detected in urine extracts using the technique commonly known as "mass fragmentography"[8] (Fig. 4), the rapid accelerating voltage switching between values required to focus fragment ions characteristic of a particular compound during the course of gas chromatographic elution. This was effected for the tri-PFP derivative of salsolinol using m/e 617 (M$^+$) and 602 (M-15) ('Varian-MAT 311' by 3% OV-1) and m/e 617 and 603 (MS-12 by 3% OV-17) and as the tri-TMS derivative using m/e 380 (M-15) and 381 (MS-12 by 3% OV-1). The penta-PFP derivative of tetrahydropapaveroline was detected by single ion monitoring of the base peak, m/e 602 ('Varian-MAT 311' by 3% OV-1) and m/e 603 (MS-12 by 3% OV-17) and as the penta-TMS derivative monitoring m/e 380 and 381 (MS-12 by 3% OV-1). These data appear to provide substantial evidence for the presence of the alkaloids in urine.

It is not yet possible to isolate a sufficient amount of each from urine for complete mass spectra to establish their absolute identity. Thus a finite (but for salsolinol, at least, extremely remote) possibility exists that a very close analogue co-elutes and contains similar ion fragments in a similar ratio. The risk of false identification is slightly greater with tetrahydropapaveroline where the fragment ions used for detection arise from only one half of the molecule. We do not, however, entertain any doubts as to their identity.

Because of these technical difficulties such qualitative precision can only be matched quantitatively when deuterated internal standards have been synthesized[9]. Nevertheless, it seems justifiable to draw certain conclusions from our semiquantitative data. There appears to be an increase in salsolinol output in the 12 h period following ethanol ingestion (Fig. 3*a*). Ethanol may have a similar effect on tetrahydropapaveroline excretion (Fig. 3*b*), although the pattern is not so consistent and the data too fragmentary to draw valid conclusions.

The relatively small output of tetrahydroisoquinolines detected during the present series of experiments gives little indication of total production and may well represent but a small fraction of the whole. The alkaloids identified may be short-lived intermediates in a system changing rapidly by routes of metabolic degradation which may be numerous and complex. An attempt to identify possible conjugation pathways by the use of a sulphatase/glucuronidase preparation ("Suc d'*Helix pomatia*") was not successful; the prolonged period of incubation involved resulted in breakdown of the compounds. Hydrolysis was therefore carried out by heating in a boiling water bath (*p*H 1, 20 min) portions of (*a*) all four fresh urine samples and (*b*) all urine samples from patient 4 in the ethanol experiment. Internal standards of salsolinol and tetrahydropapaveroline were added to duplicates before hydrolysis to enable adjustments to be made for losses on heating. Significant increases were not observed, however, in either set of samples after hydrolysis. Unless the conditions adopted were unsuitable, neither alkaloid appears to be excreted to any large extent as a sulphate or glucuronide conjugate.

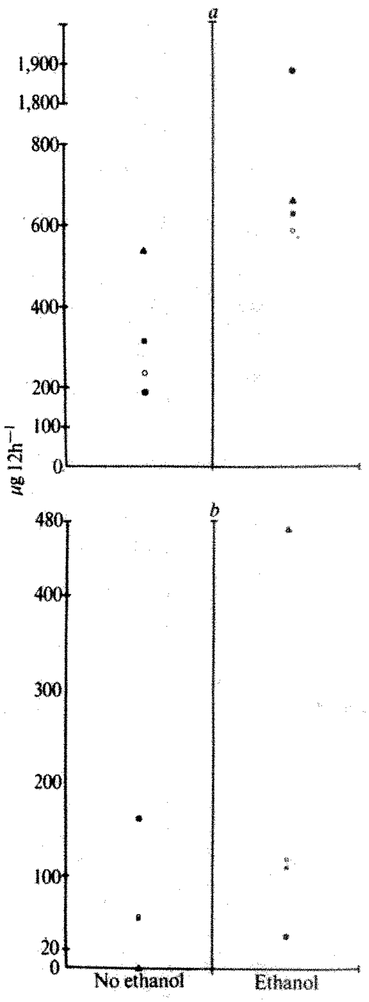

Fig. 3 Urinary excretion of (*a*) salsolinol and (*b*) tetrahydropapaveroline (μg 12 h^{-1}) before and after ethanol ingestion (see text). Each symbol represents a different subject.

The Pictet-Spengler Reaction

The Pictet-Spengler reaction involves the condensation of β-arylethylamines with carbonyl compounds[2]. Only amines with a sufficiently high electron density at the point of ring closure will cyclize with an aldehyde, as in the present experiment, to form a 1,2,3,4-tetrahydroisoquinoline. This molecular prerequisite is fulfilled with 3-hydroxylated β-phenylethylamines and with β-(3-indolyl)ethylamines. A reaction of this type is used extensively for the fluorescence histochemical localization of biogenic amines in tissues where the carbonyl agent used is formaldehyde gas[10].

Dopamine, of the biogenic amines which have so far been investigated, enters into the most rapid *in vitro* reaction with acetaldehyde[11,12]. By demonstrating unequivocally the urinary excretion of salsolinol, we have now been able to show that this reaction occurs similarly *in vivo*.

Salsolinol

Although the presence of urinary salsolinol after ethanol ingestion conformed with prediction, we were surprised to detect a relatively high output of alkaloid in these dopa-treated patients even before ethanol administration. This finding suggests an endogenous source of circulating acetaldehyde, the origin of which is speculative at the present time. There is evidence that ethanol is formed endogenously in rat, rabbit and man[13-15], perhaps in the gastrointestinal tract, and this seems to be the most likely source of this acetaldehyde. Urinary salsolinol output after L-dopa administration thus presumably mirrors endogenous acetaldehyde production and may be useful on this account. Even in the absence of exogenous L-dopa, trace amounts of salsolinol may be excreted. In the urine of two young normal adult subjects, one male and one female, small peaks were present in the appropriate position on the chromatogram corresponding, respectively, to excretion values of 29 and 25 μg per 24 h; their identity has not yet been confirmed mass spectrometrically.

Relatively little is known of the pharmacology of salsolinol. Both it and its analogue formed from the condensation of dopamine and formaldehyde seem to possess certain properties in common with the catecholamines (see ref. 4). It is entirely possible that the formaldehyde analogue itself is synthesized *in vivo*; there are indications that methanol, the formaldehyde precursor, is generated in the organism[15-17] in a similar manner to ethanol[13-15] although the function of both is quite unknown.

Tetrahydropapaveroline

Tetrahydropapaveroline was first studied by Laidlaw[18] who identified its hypotensive action in the experimental animal. This action has since been studied by others who have also shown that the compound is a β-adrenergic agonist (see ref. 4).

Hypotension, as an important and occasionally severe side-effect of L-dopa therapy in parkinsonism, has been the subject of considerable interest and speculation. There is evidence to support a central mechanism (see ref. 1), but Calne *et al.*[19] found that hypotension was a less prominent feature of the presumably wholly central clinical response of patients treated with L-dopa plus a peripheral decarboxylase inhibitor. Whether the "peripheral" component derives directly from some action of dopamine itself[20], or one of its metabolites, remains to be decided.

The complex actions of dopamine on the human circulatory system have been the subject of a recent review[21]. Its effect is predominantly on the α-adrenergic receptor, but it also acts on specific dopamine receptors in the renal and mesenteric vasculature. In addition, although to a lesser extent, it stimulates β-adrenergic receptors, and in view of our results it seems quite possible that the generation of tetrahydropapaveroline contributes to, or is responsible for, such an effect.

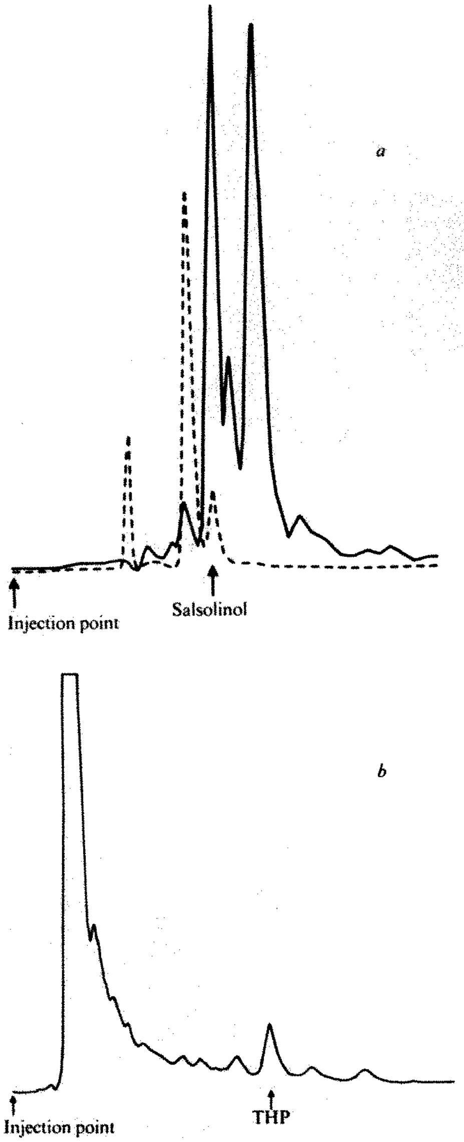

Fig. 4 Mass fragmentographic recordings of (*a*) m/e 617 (- - -) and m/e 602 (——) used to identify the tri-PFP derivative of salsolinol and (*b*) m/e 602 used to identify the penta-PFP derivative of tetrahydropapaveroline (THP) extracted from the urine of a parkinsonian patient during L-dopa therapy (Varian-MAT 311 by 3% OV1). The times of elution and, in the case of salsolinol, the ratio of the two ions, agreed with those of the PFP derivatives of authentic standards of salsolinol and tetrahydropapaveroline run on the same system.

It has been known for many years that there is a peripheral component to parkinsonian tremor; this physical sign is potentiated both by emotional tension and adrenaline administration, an effect unmitigated by the α-adrenergic blocking drug phentolamine, but abolished by β-blockade[22]. Very occasionally, L-dopa may precipitate an acute, transient episode of parkinsonian tremor with simultaneous relief of rigidity and akinesia[23]. There are indications that β-blockade with propranolol in affected patients on L-dopa treatment has a specific attenuating effect on tremor[24,25]; thus it might conceivably act by countering the effect of the β-adrenergic agonist tetrahydropapaveroline, generated peripherally.

Whether tetrahydropapaveroline is taken up, stored and discharged from catecholamine binding sites in a similar manner to the simpler tetrahydroisoquinolines[4] is unknown. There has been much speculation, however, in two areas, largely based on the resemblance of its molecular structure to certain morphine-related alkaloids, particularly apomorphine (Fig. 5). It has been suggested that potentially addictive alkaloid derivatives of this type, derived from the interaction between biogenic amines and the ethanol metabolite, acetaldehyde, form the biochemical basis of ethanol addiction, although the resemblance between opiate and ethanol addiction is not very close (see ref. 4). Tetrahydropapaveroline, or a compound resembling it, has been suggested[3] as the missing metabolite of L-dopa to account for some of the discrepancies associated with a "dopamine replacement" hypothesis of L-dopa action. Scheckel *et al.*[26] suggested that the unknown catecholamine-like material they detected in rat brains treated with dopa plus a peripheral decarboxylase inhibitor was a compound of this type, but their preliminary observations have never been followed up. In view of our results, it is obviously important to search for tetrahydropapaveroline in the brains of parkinsonian subjects who had received L-dopa. In this discussion, it is of particular interest to note that apomorphine itself leads to significant benefit in parkinsonism (see ref. 1). Unlike dopa, however, the most prominent early effect of which is the alleviation of akinesia, its most striking therapeutic action seems to be on tremor. Indeed, there is increasing evidence that L-dopa and apomorphine may have a synergistic action (e.g. ref. 27). In the light of our data, a working hypothesis that dopamine plus tetrahydropapaveroline and/or other related compounds in the Schiff base series generated at a slower rate is responsible for L-dopa action in parkinsonism seems credible. The question of whether the tetrahydroisoquinolines contribute, in addition, to normal brain function must also now be considered.

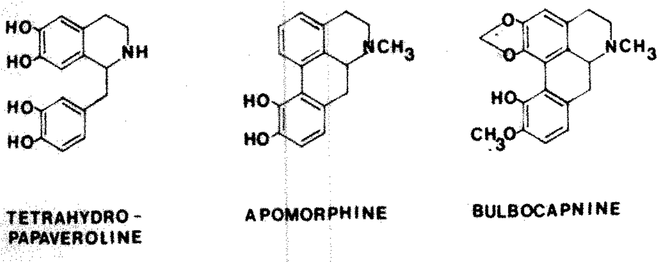

Fig. 5 Structures of the morphine-related alkaloids, apomorphine and bulbocapnine, showing their resemblance to tetrahydropapaveroline.

Schizophrenia

In his important theoretical paper, Sourkes[3] drew attention to the similarity between the molecules of apomorphine and bulbocapnine (Fig. 5) and their possible relationship to a tetrahydropapaveroline-like precursor. Thus it is quite conceivable that bulbocapnine, which produces a catatonia-like state in the experimental animal[28], may also act on central dopamine receptors in an opposite manner to that of dopamine and apomorphine[29]. This experimental catatonia is somewhat reminiscent of one manifestation of schizophrenia; it is interesting, therefore, that L-dopa tends to bring about deterioration in schizophrenic subjects[30]. Study of tetrahydroisoquinoline metabolism in schizophrenics might well be rewarding. It is even possible that another type of mental disorder, that associated with phenylketonuria, originates from the disproportionate presence of a carbonyl agent, phenylpyruvic acid, which may form a complex with a biogenic amine such as dopamine[12]. Our observations could lead to important new developments in neurological research.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Global Inventory and Distribution of Fallout Plutonium

PLUTONIUM isotopes, Pu-239,240 and Pu-238 in particular, have been injected into the stratosphere as a result of atmospheric nuclear weapons tests, and have reached the ground as particulate fallout. An accidental stratospheric injection of Pu-238 in 1964 resulted in almost a three-fold increase in the global fallout of this isotope, and we now describe the accumulated fallout and geographical distribution from this unexpected release as well as from weapons testing.

On April 21, 1964, a Transit navigational satellite was launched from Vandenburg Air Force Base in California. The payload included a Systems for Nuclear Auxiliary Power generator, SNAP-9A, containing 17 kCi or about 1 kg of Pu-238[1,2]. Because the rocket failed to boost the satellite into orbital flight, the payload re-entered the atmosphere in the Southern Hemisphere[2,3].

Subsequent stratospheric checks[4-6] indicated that the generator completely burned up during re-entry and turned into small particles at an altitude of about 50 km[4]. Concentrations of the SNAP Pu-238 in the stratosphere were measurable at the end of 1970 when it was estimated that less than a kCi remained above 12 km[7]. Attempts to measure the ground deposition rate on a continuous basis using a global fallout network were unsuccessful[8]. We finally used soil sampling to obtain integrated fallout samples, having previously demonstrated that soil at properly selected sites serves as a good indicator of cumulative fallout[9].

The stratospheric inventories clearly indicated that by mid-1970, 95% of the SNAP Pu-238 was deposited on the Earth's surface. It was important to find out how it was distributed and to record the ground deposit. Knowledge of the fate of this debris is pertinent to studies of nuclear explosions in the upper atmosphere and the use of nuclear power sources in space.

In October 1970 until January 1971, 65 sites around the world were sampled by HASL personnel and scientists from other countries; soils were collected from undisturbed areas. Each sample consisted of ten 8.9 cm diameter cores taken to 30 cm depth, representing a surface area of 622 sq. cm. The measured Pu-238 included that from weapons testing plus the SNAP-9A contribution. The Pu-239,240 was assumed to be entirely derived from weapons testing.

In order to measure the total Pu-238 with a counting error (σ) of less than or equal to ±10% 1,000 g aliquots of soil were required. An acid leaching procedure[10] used to accommodate this large size sample was found to be equally efficient[11] to complete dissolution.

The soil data are given in Table 1. The weapons Pu-238 contribution was obtained by multiplying the Pu-239,240 values by 0.024 (the average weapons Pu-238 to Pu-239,240 ratio found for six soils collected before fallout from the SNAP-9A). These soils were selected to cover a range of latitudes from 71° N to 35° S and the standard deviation of this average ratio was only ±12%. The SNAP-9A Pu-238 is then simply the difference between the total measured Pu-238 and the weapons Pu-238.

The sites in Table 1 were grouped into ten degree latitude bands and the deposition values averaged. We plotted these averages against the sine of the latitude and made straight line extrapolations to zero at the poles. The average activities per square km in each ten degree latitude band are given in Table 2. The error term associated with the average for each ten degree latitude band is simply the standard deviation when two or more sites are located in the same band. Where only one site is represented or the value was derived by extrapolation, an average error for other bands in the hemisphere was applied.

The distribution pattern for weapons' plutonium shows heaviest deposition in the Northern Hemisphere temperate latitudes and a minimum in the equatorial region. There is a

Table 1 Pu Isotopes in Soil Collected 1970-71

Country	Site	Lat.°	Avg. annual precip. (cm)	mCi per km^2 Pu-239,240	mCi per km^2 Pu-238 Weapons	mCi per km^2 Pu-238 SNAP-9A
			Northern Hemisphere			
Greenland	Thule	76.6	<15	0.33	0.008	(0.001)
USA	Barrow, Alaska	71.3	14	0.40	0.010	(0.004)
USA	Fairbanks, Alaska	64.8	28	0.85	0.020	0.020
Iceland	Reykjavik	64.1	86	1.5	0.036	0.016
USA	Palmer, Alaska	61.6	41	0.92	0.022	0.022
Norway	Bergen	60.4	192	3.1	0.074	0.049
Norway	Oslo	59.9	76	1.5	0.036	0.010
UK	Wick, Caith.	58.4	80	1.4	0.034	0.014
Denmark	Roskilde	55.6	59	1.2	0.029	0.009
UK	Wantage, Berks.	51.6	68	1.1	0.026	0.019
Germany	Munich	48.1	87	2.8	0.067	0.021
USA	Puyallup, Wash.	47.2	109	1.4	0.034	0.012
Italy	Ispra	45.8	145	2.5	0.060	0.025
USA	Orono, Maine	44.9	94	1.7	0.041	0.016
Japan	Sapporo	43.1	118	1.9	0.046	0.026
USA	Vermillion, S.D.	42.8	65	2.3	0.055	0.049
USA	Argonne, Ill.	41.8	84	2.1	0.050	0.019
USA	New York, N.Y.	40.8	90	2.6	0.062	0.035
USA	Salt Lake City, Ut.	40.8	40	2.6	0.062	0.032
USA	Denver, Colo.	39.8	38	1.8	0.043	0.034
USA	Manhattan, Kan.	39.2	77	2.4	0.058	0.029
Portugal	Sacavem	38.8	73	1.5	0.036	0.012
USA	Tulsa, Okla.	36.2	94	2.2	0.053	0.038
USA	Raleigh, N.C.	35.8	116	2.4	0.058	0.047
Japan	Tokyo	35.7	152	1.5	0.036	0.018
USA	Burbank, Calif.	34.2	26	0.73	0.018	0.003
Pakistan	Lahore	31.6	49	1.6	0.038	0.018
USA	Kingsville, Tex.	27.5	63	0.99	0.024	0.008
USA	Ft. Pierce, Fla.	27.5	142	1.0	0.024	0.010
USA	Weslaco, Tex.	26.2	61	0.88	0.021	0.016
USA	Papaikou, Hawaii	19.8	400	4.0	0.096	0.027
Venezuela	Maracay	10.3	96	0.24	0.006	0.003
Colombia	Bogota	4.6	106	0.13	0.003	(0.001)
			Southern Hemisphere			
Kenya	Muguga	1.2	96	0.52	0.012	0.011
Brazil	Belem	1.5	268	0.42	0.010	0.019
Ecuador	Guayaquil	2.2	110	0.18	0.004	0.004
Angola	Luanda	8.8	43	0.093	0.002	0.006
Peru	Lima	12.1	4	0.12	0.003	0.015
Australia	Darwin	12.4	158	0.28	0.007	0.074
Mozambique	Nampula	15.2	102	0.15	0.004	0.026
Rhodesia	Salisbury	17.7	83	0.16	0.004	0.022
Australia	Townsville	19.2	119	0.18	0.004	0.046
Mozambique	Beira	19.8	151	0.17	0.004	0.036
Australia	Port Hedland	20.3	31	0.20	0.005	0.017
Brazil	Rio de Janeiro	22.9	150	0.61	0.015	0.148
Brazil	Angra dos Reis	23.0		0.60	0.014	0.098
Australia	Alice Springs	23.7	24	0.35	0.008	0.071
S. Africa	Pretoria	25.8	76	0.32	0.008	0.052
Mozambique	Lourenco Marques	26.0	80	0.25	0.006	0.043
Australia	Brisbane	27.4	108	0.40	0.010	0.061
Australia	Perth	33.1	102	0.41	0.010	0.056
Chile	Santiago	33.5	36	0.22	0.005	0.043
S. Africa	Stellenbosch	33.9	70	0.26	0.006	0.031
Australia	Sydney	34.8	144	0.47	0.011	0.050
Argentina	Buenos Aires	34.8	99	0.49	0.012	0.081
Australia	Adelaide	35.2	88	0.33	0.008	0.078
New Zealand	N. Aukland	35.8	181	0.43	0.010	0.086
Australia	Melbourne	38.2	103	0.55	0.013	0.065
Chile	Puerto Montt	41.5	260	0.20	0.005	0.057
Australia	Hobart	41.5	83	0.26	0.006	0.045
New Zealand	Greymouth	42.5	250	0.67	0.016	0.126
New Zealand	S. Canterbury	44.4	57	0.28	0.007	0.048
Chile	Punta Arenas	53.2	22	(0.19)	(0.004)	(0.034)

Table 2 Average Latitudinal Distributions of Cumulative Pu-239,240 and Pu-238 Fallout

Hemisphere	Lat. band°	mCi per km² Pu-239,240	Pu-238 Weapons	Pu-238 SNAP-9A
Northern	90–80	(0.10 ± 0.04)	(0.002 ± 0.001)	(< 0.001)
	80–70	0.36 ± 0.05	0.009 ± 0.001	< 0.001
	70–60	1.6 ± 1.0	0.038 ± 0.025	0.026 ± 0.015
	60–50	1.3 ± 0.2	0.031 ± 0.004	0.013 ± 0.004
	50–40	2.2 ± 0.5	0.053 ± 0.011	0.026 ± 0.011
	40–30	1.8 ± 0.6	0.042 ± 0.014	0.025 ± 0.015
	30–20	0.96 ± 0.07	0.023 ± 0.002	0.011 ± 0.004
	20–10	0.24 ± 0.10	0.006 ± 0.002	0.003 ± 0.002
	10–0	0.13 ± 0.06	0.003 ± 0.001	< 0.001
Southern	0–10	0.30 ± 0.20	0.007 ± 0.005	0.010 ± 0.007
	10–20	0.18 ± 0.05	0.004 ± 0.001	0.036 ± 0.021
	20–30	0.39 ± 0.16	0.009 ± 0.004	0.070 ± 0.042
	30–40	0.40 ± 0.12	0.009 ± 0.003	0.061 ± 0.020
	40–50	0.35 ± 0.21	0.008 ± 0.005	0.069 ± 0.038
	50–60	(0.20 ± 0.09)	(0.005 ± 0.002)	(0.044 ± 0.023)
	60–70	(0.10 ± 0.04)	(0.002 ± 0.001)	(0.022 ± 0.012)
	70–80	(0.03 ± 0.01)	(0.001 ± 0.001)	(0.008 ± 0.005)
	80–90	(0.01 ± 0.004)	(< 0.001)	(0.004 ± 0.002)

Results in parentheses were derived by extrapolation; error terms are standard deviations.

slight rise in the Southern Hemisphere temperate zone which, at its peak, is about one-fifth of the Northern Hemisphere maximum. The SNAP-9A Pu-238 has an entirely different distribution pattern. Most of the SNAP debris has deposited in the Southern Hemisphere where the maximum fallout is 2.5 times that in the Northern Hemisphere.

Table 3 Inventory of Pu-239,240 and Pu-238 Fallout

	kCi deposited Pu-239,240	Pu-238 Weapons	Pu-238 SNAP-9A
Northern Hemisphere	256 ± 33	6.1 ± 0.8	3.1 ± 0.8
Southern Hemisphere	69 ± 14	1.6 ± 0.3	10.8 ± 2.1
Global	325 ± 36	7.7 ± 0.9	13.9 ± 2.2

The average and extrapolated activities per square km for each ten degree latitude band were multiplied by the latitude band area to calculate the total deposit in kCi. These values were then summed to obtain the inventories in Table 3. The errors were propagated by conventional means.

The total Pu-239 deposit was 326 ± 36 kCi and the weapons Pu-238, 7.7 ± 0.9 kCi. Our estimate of the SNAP-9A Pu-238 deposit, 13.9 ± 2.2 kCi, is in reasonable agreement with the 16 kCi we would expect to have fallen out based on the stratospheric inventory. Over 75% of the total SNAP Pu-238 deposit is in the Southern Hemisphere whereas only about 20% of the total weapons Pu-238 fallout occurred in that hemisphere. This accidential release of Pu-238 almost tripled the global deposit of this plutonium isotope by 1970. The distributions and inventories of the weapons Pu-238 and Pu-239,240 are in reasonable agreement with estimates based on Sr-90 deposition and Pu-239,240 to Sr-90 ratio measurements[12].

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Electron Microscopy of Monomolecular Layers of Thorium Atoms

IMAGES of heavy atoms in single molecules have recently been obtained with scanning transmission electron microscopes as well as conventional electron microscopes in both bright and dark-field operation[1–4]. Because of the random orientation of isolated molecules on the specimen support, only a few of them show the true interatomic distances in parallel projection. Also molecules could stack themselves during preparation. Finally, the limited depth of focus of electron microscopes at 100 kV when viewing atoms[5] makes it necessary to obtain a flat specimen.

To overcome these difficulties it is necessary to prepare monomolecular films 6–30 Å thick. Such monolayers of atoms can be formed on liquid-air interfaces in Langmuir troughs and it is possible to obtain different molecular structures with the molecules tagged with heavy atoms. For electron micro-

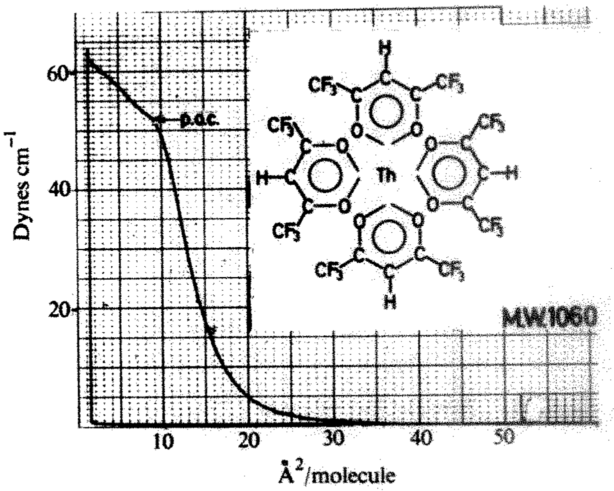

Fig. 1 Isotherm of thorium–hexafluoracetylacetonate at 3° C. p.o.c., Point of collapse.

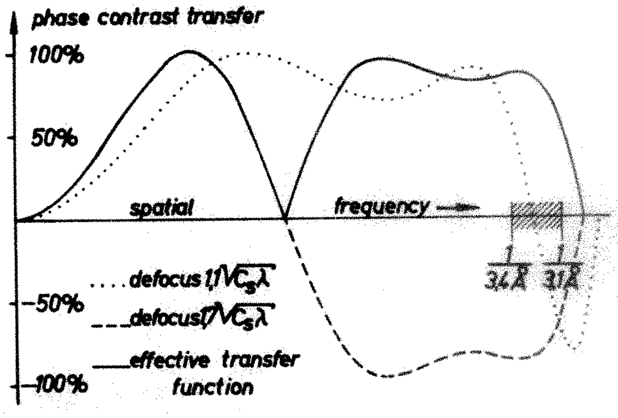

Fig. 2 Phase contrast transfer functions for $C_s = 1.32$ mm, $C_c = 1.62$ mm, $\lambda = 0.037$ Å (100 kV) and Maxwellian velocity distribution at $T = 2,900$ K.

scopy (EM) test specimens with single heavy atom patterns of controllable spatial frequency can be obtained. Discrimination between elements[6] can be tested using arrays of atoms with different atomic numbers and so any damage caused by irradiation should be detected directly.

Monolayers or bilayers are of considerable biological relevance as they are similar to the molecular arrangement in cell membranes and may provide structural information on molecular interactions at interfaces.

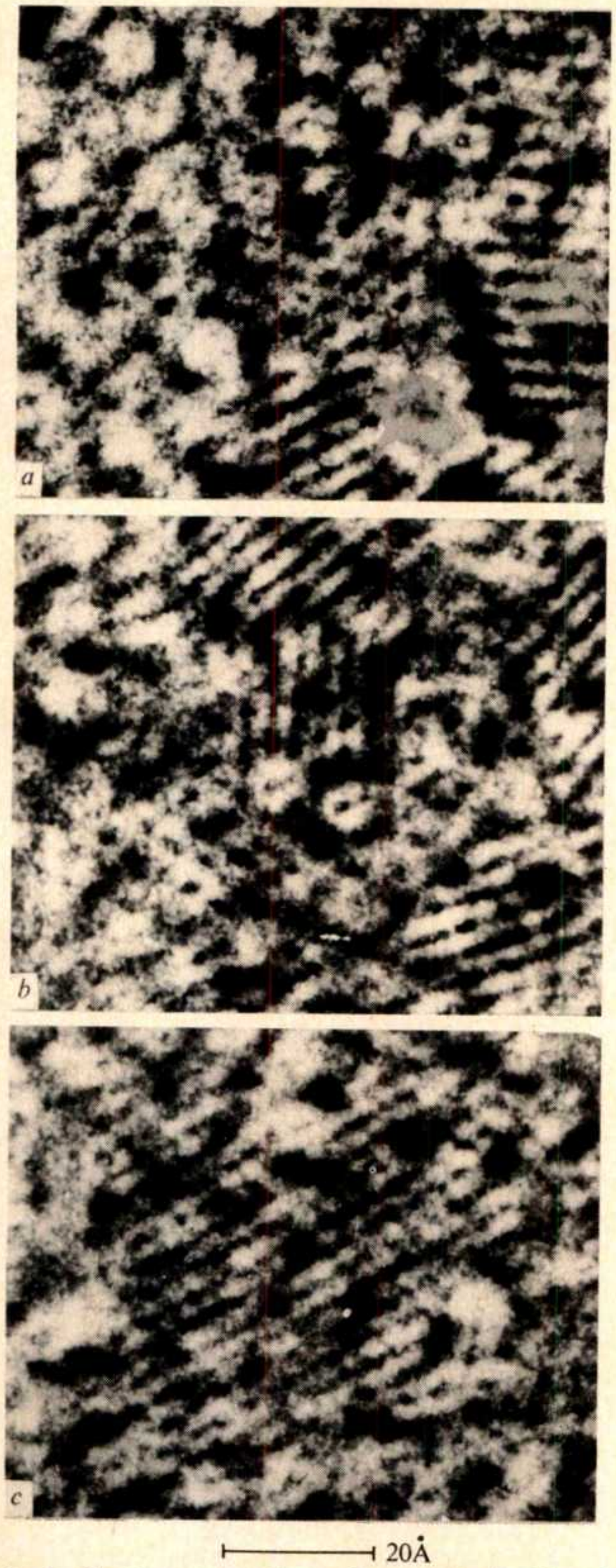

Fig. 3 Thorium atom patterns of monomolecular film of thorium–hexafluoracetylacetonate on a support of thin carbon. Electron micrographs: 4.3×10^5 magnification; prints at magnification of 10^7.

We used a specially designed Langmuir trough to generate monomolecular films and to transfer them to specimen supports for investigation by an electron microscope. A pressure-sensing float and a barrier driven by a motor, each fencing the film and connected to a recorder *via* amplifiers and interconnected by a feedback-loop, made it possible, first, to obtain isotherms of films to survey their performance and, second, to maintain any selected pressure of the film during transfer to the specimen support[7].

Preliminary transfer experiments showed the wettability of supports used for specimens and radiation damage to be critical factors[8]. To prove the feasibility of electron-optical imaging of heavy atom patterns we transferred a monolayer of thorium–hexafluoracetylacetonate to a carbon film—thus combining a high atomic number element with a structure of low radiation sensitivity on a sufficiently wettable support. The isotherm for 3° C (Fig. 1) reaches the point of collapse at 52 dyne cm^{-1} and a mean area of 9 Å^2 per molecule. We transferred this monolayer at 32 dyne cm^{-1} and expected interatomic distances between 3.1 Å and 3.3 Å in a hexagonal array judging from the Archimedean square antiprismatic structure of the molecule[9].

Electron micrographs were obtained at 100 kV with a Siemens Elmiskop 101 equipped with special objective lens (spherical aberration $C_s = 1.32$ mm; chromatic aberration $C_c =$ 1.62 mm) and improved stability of lens current and high tension supplies.

The chief source of contrast in high resolution electron microscopy is the interference of the diffracted wave, whose phase is changed by the field of the atomic nucleus, with the undiffracted wave. Therefore spatially coherent illumination is used and the properties of the objective are given by coherent phase transfer functions dependent on spherical aberration and defocus. Obviously the expected spatial frequencies around 3.2 Å^{-1} would not be properly imaged at the commonly used Scherzer defocus $1.1 \times \sqrt{C_s\lambda}$ (ref. 10) because of the zero crossing of the respective transfer function (see Fig. 2). Therefore we used the second main transfer interval[11] at a defocus of $1.7\sqrt{C_s\lambda}$ which, of course, makes the "atom"-dot in the picture to be bright. To restore readability of the images and to improve resolution and contrast, we processed our micrographs by spatial filtering of the Maréchal type[12], which effectively reverses the negative lobe of the transfer function. Fig. 3 shows prints of the processed micrographs taken at 435,000 times the primary magnification enlarged to 10^7 magnification. Small areas of undisturbed monolayer with single heavy atom pattern can be recognized. As the surface of the supporting carbon film is not smooth, the monolayer is obviously broken up into many small panels. If these are not nearly perpendicular to the optical axis, their frequencies are raised by tilted projection into the zero-crossing region of the transfer function. Therefore some atom rows do not appear as single dots.

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Migration of Trace Metals in Snow

SEVERAL workers[1-4] have established that elemental mercury vapour is present in soils overlying mineralized bedrock, and the vapour can be used in prospecting for base metal sulphide deposits[5]. It is therefore possible that mercury vapour will emanate from soils into overlying snows and that the trace metals in fallen snow can be used to indicate the presence of underlying, or at least nearby, mineralization. Kolotov and colleagues[6] have already reported the presence of such dispersion aureoles for zinc, copper and lead, as total heavy metals, in snow above a deposit of tin ore, but they ascribe the phenomenon to falling snow carrying down dust clouds which were thought to exist over the deposit.

Various mechanisms by which metals may be trapped in snow have been tested by taking samples in three types of environment—urban, unmineralized rural and mineralized rural. Snows were sampled in the city of Ottawa and in the vicinity of a mercury prospect near Clyde Forks in Eastern Ontario. At the latter site, mineralization consists of veinlets of chalcopyrite, tetrahedrite and pyrite with which are associated the metals, copper, mercury, lead, zinc and manganese. The same metals are also dispersed to some extent in overlying soils. Snow was collected over these soils and also in areas remote from mineralization.

The analytical data presented represent whole snow samples. Melt water was coarsely filtered ('Whatman 30') to remove gross contaminants. Cu, Zn, Pb, Cd and Ni were determined by atomic absorption spectrometry after extraction with methyl iso-butyl ketone and APDC. Mn, Na, K, Fe and Hg were similarly determined but without previous extraction.

In January 1971, fresh fallen snow samples collected in Ottawa were shown to contain 3.5 to 4.0 p.p.b. Hg (parts per thousand million) with a mean of 3.7 p.p.b. The snow contained scattered soot particles which are thought to be residues of burned fuel-oil and gasoline. The elevated Hg values probably reflect the low, but in this case significant, Hg content of fossil fuels[7].

In January 1972, snow samples from the same area unaccountably showed much less Hg but did contain a variety of other metals. Analytical data are presented in Table 1.

I consider that the prime influence on these metal contents is the proximity of a 6-lane freeway. Sample 3 was collected closest to the road (100 yards). The others were further removed (500 yards). Roads in the Ottawa area are salted during winter snowfalls causing heavy traffic to raise a mist of melt water into the atmosphere above them. Elevated contents of Na, Zn, Pb, Ni and Fe in nearby fallen snow clearly support the contention that falling snow is an efficient scavenger of airborne dust and aerosols.

Table 1 Trace Metal Contents of Snow from an Urban Area

Sample No.	Hg (p.p.b.)	Cu (p.p.b.)	Zn (p.p.b.)	Pb (p.p.b.)	Ni (p.p.b.)	Cd (p.p.b.)	Na (p.p.m.)	K (p.p.m.)	Fe (p.p.b.)
1	0.065	17	22	87	21	0.3	17	1.2	90
2	0.071	15	18	55	20	<0.2	32	2.5	30
3	0.123	21	192	410	17	1.0	328	0.9	130
4	0.071	69	27	78	10	0.7	3	0.4	—

For rural areas the data in Table 2 show that the metal contents of fresh surface snow in unmineralized areas are much less than in Ottawa. These figures probably represent normal background levels in the atmosphere. However, snow strata collected in mineralized zones contain significant Hg, Pb, Zn, Cu and Mn (Table 2) particularly in sub-surface samples near to the soils. I considered that these and probably other metals readily migrate upwards into the snow strata from underlying mineralized soils to reach the levels indicated in less than 2.5 months. Significant concentration gradients are observed only for the major ore metals, Hg and Cu, where 40 to 50-fold differences in metal content are observed across a 5 foot depth of snow. Gradients measured for the minor ore metals, Zn, Pb and Mn, are by comparison quite low and similar to those measured at an unmineralized site. They therefore represent migration from soils with common background contents of these metals (Table 3).

Table 2 Trace Metals in Snow

Snow horizon depth (in feet) from snow surface		Hg	Cu	Zn	Pb	Mn
Samples from an unmineralized site						
Surface	0–1	<0.01	3	8	5	<15
Middle	1–2	<0.01	4	15	15	<15
Lower	3–4.5	<0.01	8	16	12	<15
Total depth, 5 feet						
Samples from a mineralized site						
Surface	0–1	<0.01	3	12	9	<15
	1–2	0.40	27	28	11	<15
Middle	2–3	0.19	73	14	10	<15
	3–4	0.30	74	182	2	15
Lower	4–5	0.52	98	18	4	20
Total depth, 5 feet						

All values in p.p.b. (parts per thousand million).

Table 3 Trace Metals in Soils

Soil description	Hg	Cu	Zn	Pb	Mn
Humic soil overlying mineralization	278	370	65	12	910
Mineralized gravels	1,200	11,800	400	20	1,030
Humic soil from an unmineralized zone	0.38	31	220	55	1,600
Mineralization is covered by 1 to 2 feet of soils					

All values in p.p.m.

The migration mechanism in this case is probably related to the upward movement of pellicular waters which carry metal ions and perhaps humate complexes from the soils into the overlying snow strata. Mercury may also migrate as dissolved elemental vapour.

It is worth noting that the trace metal levels found in snow in each situation are comparable. The presence of elevated metal levels may therefore be regarded as man-made contamination in the first case and as natural contamination in the second case.

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Thermal Radiation from a Tropospheric Dust Suspension

INCREASING concern is being felt by scientists and laymen alike over the possibility of climate alteration due to increased atmospheric dust. Although the early consensus of most scientists was that increasing the dust content of the atmosphere would tend to cool the Earth, owing to an increased backscatter to space of solar radiation, several investigators have recently published studies indicating that this conclusion may not unconditionally hold true[1–3]. Thus, the question of whether increased atmospheric aerosol would tend to warm or cool the Earth, *via* its interaction with solar radiation, remains an open one, awaiting additional data on the solar scattering and absorptive properties of natural and man-made aerosols.

A second approach to the question, however, is to consider the interaction of atmospheric aerosol with long-wave terrestrial radiation. Although practically all previous studies considered this interaction to be negligible[3,4], there have been some recent experimental indications that quite the opposite may be true[5–7]; and in this paper I report on one additional example.

On the evening of July 29, 1972, a huge but weak dust storm hit Phoenix, Arizona, at about 2000 MST (Mountain Standard Time), and shortly thereafter exhausted itself over the metropolitan area. The finer residue of the dust remained in suspension through most of July 30, reducing visibilities from 52 to 8 km. Dust storms of this type at Phoenix generally raise a surface dust cloud that extends to a height of 2,500 m (ref. 8); and the dust suspension of July 30 was estimated to extend to at least this height, which is also the level of the mean maximum mixing height at that time of year[9].

July 30 was a cloudless day, and atmospheric thermal radiation measurements were collected from 1000 MST until 1500 MST, when the dust began to move out of the instrument area. These data were obtained by subtracting the solar radiation measured by a temperature compensated Eppley pyranometer from the mean hemispherical all-wave radiation obtained from three Fritschen-type net radiometers[10,11] converted to hemispherical operation by the technique of Idso[12,13]. The results are shown in Table 1 together with measurements on three other adjacent cloudless days, screen-level air temperature and vapour pressure, and mean wind speed and visibility. The visibility data give an indication of the relative clarity of the three normal cloudless days as compared to July 30; and the wind speed data show the potential of all days for similar temperature profiles in the boundary layer.

Using the Brunt equation[14] to estimate the effects on the atmospheric thermal radiation of the reduced air temperature but increased vapour pressure of July 30 compared with the

Table 1 Air Temperature, Vapour Pressure, Visibility, Wind Speed and Atmospheric Thermal Radiation on Three Normal Clear Days (July 27, 31; August 1) and the Day of the Dust Suspension (July 30)

Parameter	Time	1000	1030	1100	1130	1200	1230	1300	1330	1400	1430	1500	Av.
Air temperature (°C)	July 27	37.2	38.0	38.2	41.1	39.7	40.8	43.8	45.7	44.8	44.3	43.4	41.5
	July 31	39.1	39.4	44.8	44.3	43.8	45.0	45.0	45.9	44.6	43.4	45.9	43.7
	August 1	39.4	42.9	43.8	43.6	44.0	44.8	45.5	46.6	45.7	48.0	45.5	44.5
	Average	38.5	40.1	42.3	43.0	42.5	43.5	44.8	46.1	45.0	45.2	44.9	43.2
	July 30	38.2	40.3	39.7	41.1	41.9	42.9	42.2	41.9	43.4	43.4	44.6	41.8
Vapour pressure (mbar)	July 27	18.4	19.2	18.1	21.1	16.0	16.9	15.3	17.0	15.2	14.8	14.1	16.9
	July 31	15.5	15.7	19.9	19.4	17.1	18.2	16.3	17.1	15.0	14.1	14.1	16.6
	August 1	12.9	15.5	15.3	15.2	13.6	14.2	12.8	13.5	13.9	15.6	12.8	14.1
	Average	15.6	16.8	17.8	18.6	15.6	16.4	14.8	15.9	14.7	14.8	13.7	15.9
	July 30	17.4	19.5	18.2	19.6	19.6	20.6	18.2	18.0	18.5	18.5	17.8	18.7
Visibility (km)	July 27	48		48		48		48		48		56	49
	July 31	48		48		48		48		48		48	48
	August 1	56		56		56		56		64		64	59
	Average	51		51		51		51		53		56	52
	July 30	8		6		8		8		8		10	8
Wind speed (m s^{-1})	July 27	1.0		2.1		3.1		3.6		5.1		2.6	2.9
	July 31	1.5		3.1		2.6		3.6		5.7		3.6	3.4
	August 1	3.6		2.1		2.6		4.6		4.6		4.6	3.7
	Average	2.0		2.4		2.8		3.9		5.1		3.6	3.3
	July 30	1.5		5.1		3.6		4.1		4.1		5.7	4.0
Thermal radiation (cal cm^{-2} min^{-1})	July 27	0.762	0.756	0.757	0.746	0.760	0.748	0.770	0.777	0.772	0.772	0.750	0.761
	July 31	0.766	0.779	0.706	0.732	0.771	0.774	0.791	0.776	0.774	0.774	0.761	0.764
	August 1	0.736	0.784	0.737	0.760	0.765	0.772	0.774	0.762	0.776	0.771	0.761	0.763
	Average	0.755	0.773	0.733	0.746	0.765	0.765	0.778	0.772	0.774	0.772	0.757	0.763
	July 30	0.778	0.786	0.814	0.816	0.814	0.827	0.825	0.820	0.806	0.809	0.791	0.808

other three cloudless days, it was calculated that this energy flux should have been 1.6% greater on July 30. The actual measurements showed it to be 5.9% greater, however, implying that the dust suspension of July 30 was responsible for a 4.3% increase in atmospheric thermal radiation.

That this figure is probably a very conservative estimate of the potential long-wave aerosol effects may be shown by use of the concept of effective atmospheric emittance, defined as incoming thermal radiation received per calculated blackbody radiation at measured screen level air temperature. For the three normal cloudless days the mean effective atmospheric emittance over the 1000–1500 period was 0.955. As 1.000 represents the theoretical upper limit of this parameter, it is seen that dust effects could only have increased it by 4.7%. The measured value of 4.3% differs from this potential value by an amount that is of the order of the resolution of the instrumentation employed in obtaining it. Thus, it may be concluded that the dust suspension of July 30 transformed the atmosphere into an effective blackbody, limiting any further increases in the atmospheric thermal radiation and prohibiting the experimental determination of its full potential for long-wave radiation interaction.

This point is significant in that the effective atmospheric emittance is temperature dependent, and the mean value for the Earth as a whole is much lower than that prevailing at Phoenix on the days of this study. In particular, the effective atmospheric emittance appears to have a minimum value of about 0.74 in the region of 0° C, tending towards unity at both higher and lower temperatures[15] to yield a mean value of about 0.88[16]. Thus, the long-wave effects of an atmospheric aerosol could be much greater than the 4.3% increase they effected in the atmospheric thermal radiation in this study. Indeed, measurements I made during a winter dust storm indicated that an increase in atmospheric thermal radiation of 12 to 13% may be brought about by low level dust[7].

Notwithstanding this greater potential effect, just the basic 4.3% increase in effective atmospheric emittance discovered in this study is sufficient to alter vastly the Earth's climate through the so-called "greenhouse effect". *Via* this well-known mechanism, any increase in the emissivity of the Earth's atmosphere will produce an incremental temperature rise near the planet's surface. Using the heat balance model of Haltiner and Martin[16] for mean Earth conditions, it may be calculated that the long-wave aerosol effects detected in this study could conceivably warm the Earth by 3 or 4° C. In view of the uncertainty associated with even the qualitative effects of aerosol interaction with solar radiation, these results suggest that the likely effect of increasing the dust content of the atmosphere would be to produce a warming trend at the Earth's surface.

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Tritium Contamination of Deuterium Compounds

Two reports[1,2] have appeared which indicate that various commercial deuterated reagents and solvents contain appreciable quantities of tritium. Because this matter is of concern especially in view of the wide use of deuterated compounds as solvents for n.m.r. spectroscopy I wish to report that these observations are in error. Leete[1] indicated that only the deuterium oxide (D_2O) supplied by one company was low in tritium. In fact D_2O supplied by that company before the middle of 1971 was, at times, also high in tritium, and since then D_2O supplied by most companies has been low in tritium. The US Atomic Energy Commission (AEC) is the prime source of D_2O to nearly all suppliers and the results shown in Table 1 illustrate the dramatic reduction in tritium content of recent samples of D_2O obtained from the AEC.

Table 1 Tritium Content of D_2O Received from AEC

Date	μCi ml.$^{-1}$ of D_2O
September, 1969	6.0
November, 1969	6.0
April, 1970	6.0
April, 1970	0.06
May, 1970	0.12
July, 1970	0.09
September, 1970	0.06
September, 1970	0.09
November, 1970	0.1
December, 1970	0.27
January, 1971	0.02
March, 1971	0.0012
July, 1971	0.00047
October, 1971	0.0004
January, 1972	0.0003
March, 1972	0.00031
March, 1972	0.00008
May, 1972	0.0004
August, 1972	0.00008

Thus, Leete's results (private communication) are no longer valid, having been obtained from old samples of D_2O; the heavy water currently available contains very little tritium. Because D_2O is the prime source of deuterium for other deuterated materials the reduction in the tritium content of D_2O will result in a marked decrease in the tritium content of other deuterated chemicals.

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Micro-fission Explosions and Controlled Release of Thermonuclear Energy

The possibility of igniting a thermonuclear micro-explosion by a laser pulse has recently attracted great interest as a result of the proposal to lower the energy requirements by imploding a T-D thermonuclear pellet with a laser pulse of proper shape, thereby increasing its density by a factor of $\sim 10^4$ over the solid density[1]. If this concept of high density compression is applied to a fissionable pellet, consisting of ^{235}U, ^{233}U or ^{239}Pu, very small critical masses become possible. These critical masses can be further reduced by surrounding the fissionable pellet with a neutron reflecting material to be compressed, together with the pellet, to high densities. Finally, if this neutron reflecting material consists of thermonuclear material such as T-D, the fission chain reaction rising in the critical pellet will ignite a small thermonuclear explosion in the neutron reflector. The fission chain reaction rises at a much faster rate than for solid densities (such as in atomic bombs) because of the greatly increased densities. The release of thermonuclear neutrons in the reflector will accelerate the fission chain reaction to an even higher speed whereby the heating of the thermonuclear material is accelerated in return, resulting in even more thermonuclear neutrons.

The system may be useful as a small fission power plant, especially for a safe breeder reactor or as a combined fission-fusion power plant. Another important application of this concept is for space propulsion.

In the spherical ablation implosion concept of laser fusion, pressures up to $p \simeq 10^{18}$ dyne cm^{-2} are predicted. If these pressures are applied to a solid such as ^{235}U, ^{233}U or ^{239}Pu the density can be calculated from a Thomas–Fermi equation of state. This implies densities ~ 240 times larger than solid densities with an atomic number density of $N \simeq 1.17 \times 10^{25}$ cm^{-3}.

The critical radius for a spherical mass of fissionable material is[2]

$$R_0 = \frac{\pi}{B_m} - d \qquad (1)$$

with $B_m^2 = 3\sigma_s \sigma_f N^2\ (\nu - 1)$, $d \simeq 0.71/N\sigma_s$, where $\sigma_s \simeq 2 \times 10^{-24}$ cm^2, $\sigma_f \simeq 2 \times 10^{-24}$ cm^2 are the neutron cross-sections for scattering and fission, and $\nu \simeq 2.9$ the neutron multiplication factor. From equation (1) $R_0 \simeq 2.6 \times 10^{-2}$ cm, with a pellet volume of $V \simeq 7.35 \times 10^{-3}$ cm^3. The critical mass at 240 times solid density is then $m \simeq 0.34$ gm.

The compression energy is given by $E \simeq (2/3)pV \simeq 4.9 \times 10^{13}$ erg $= 4.9$ MJ. The total energy required to reach this highly compressed state will be larger because a substantial portion of the energy will go into the ablation products. Nevertheless it is clear that the energies needed for compression are here in the same order of magnitude range as for the requirement to ignite a T-D micro-fusion explosion. Further, relativistic electron beams are already available at energies in this range and they may be similarly employed for compression; they have already been proposed as an alternative to laser fusion ignition systems[3].

For a spherical pellet surrounded by a strong neutron reflector the critical radius is[2]

$$R = \frac{3}{2} \frac{D_r}{D_c B_m^2 T} \left[1 + \left(1 + \frac{4}{3} \frac{D_c}{D_r} B_m^2\, T^2 \right)^{1/2} \right] \qquad (2)$$

where $D_c \simeq 3/N_c \sigma_{cs}$, $D_r \simeq 3/N_r \sigma_{rs}$ are the neutron diffusion coefficients in the fissionable core (D_c) and neutron reflector (D_r), σ_{cs} and σ_{rs} are the neutron scattering cross-sections in the core and reflector. If the reflector consists of T-D the atomic number density at $p = 10^{18}$ dyne cm^{-2} is $N_r \simeq 5 \times 10^{26}$ cm^{-3}. With $\sigma_{rs} \simeq 2 \times 10^{-24}$ cm^2 and for $R \simeq T$, equation (2) gives $R \simeq 4.7 \times 10^{-3}$ cm with a critical mass of $m \simeq 1.9 \times 10^{-3}$ gm. The compression energy in this case is $E \simeq (2/3)pV \simeq 2.3 \times 10^5$ J with $V = (4\pi/3)(R+T)^3$.

The fission chain reaction proceeds according to the equation

$$n = n_0 \exp\left(N\sigma_f v_0\, (\nu - 1)t\right) \qquad (3)$$

where n is the number of fission neutrons released at time t and $v_0 \simeq 10^9$ cm s^{-1} is the neutron velocity. For the numbers given above.

$$n \simeq n_0 \exp\left(4.7 \times 10^{10} t\right) \qquad (4)$$

From equation (4) the e-folding time $t_e \simeq 2 \times 10^{-11}$ s. The hydrodynamic disassembly time at keV temperatures is given by $\tau \sim R/v \sim 10^{-9}$ s. The chain reaction will have progressed during this inertial confinement time to $n \simeq n_0 e^{50} \sim 10^{22} n_0$. This very large number of neutrons delivered indicates that a very high fission yield occurs, substantially larger than that which can be achieved in atomic bombs.

In order to obtain a fast rising chain reaction the pellet must be somewhat larger than the critical dimension which in turn requires a somewhat larger energy input for compression than estimated above.

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Mercury in Lake Sediments: a Possible Indicator of Technological Growth

GOLDBERG[1] has estimated that at present man is responsible for about half of the total Hg released into the environment, and pollutant Hg has already been found in snow and ice[2] and near-shore marine sediments[3]. It seemed to us that lake sediments, which geologically have a relatively rapid rate of deposition, might produce further evidence of man's input of Hg to the environment. This has been shown to occur in sediments from a Canadian lake which receives industrial waste[4]. Our sediments are from an English lake in a predominantly rural area.

A 1 m undisturbed sediment core was obtained from the South Basin, Lake Windermere, England, using a pneumatic corer[5]. There was a transition in the sediment at ~28 cm depth; above this the sediments consisted of poorly compacted black *Asterionella* muds, and below it was a sequence of well compacted brown clays. Hg in the sediments was determined by a modification of a cold vapour atomic absorption procedure[6]. For the top ~28 cm of the core (black mud) the accumulation rate (2.7 mm yr^{-1}) of wet sediment was determined by a ^{210}Pb radionuclide technique adjusted to take account of the enhanced water content of the topmost 10 cm, and for the underlying brown clay the value given by Creer *et al.*[10] (average 0.35 mm yr^{-1}) was used. There is a stepwise increase in Hg content upwards within the core (Table 1).

Methylation of inorganic Hg by organisms can result in the release, upward movement and subsequent recycling of a volatile form of mercury. But, in the presence of methogenic microorganisms methylation is confined to the upper ~3 cm of sediment[8], and occurs at the rate of ~0.1% per year of the total Hg present. Because the sedimentation rate at the site of the present core is ~2.7 mm yr^{-1} a sediment cover of 3 cm will be supplied in ~12 yr and the loss of Hg from the layer of active methylation will be negligible and cannot account for the increase in Hg which occurs at various levels in the core.

The upward post-depositional migration of inorganic Hg through the interstitial waters by ionic or molecular diffusion, or sediment compaction, could lead to an enhancement of Hg in the upper portions of the core. On present evidence this process is difficult to assess. Thomas[4] rejects Hg mobility as a controlling factor in the distribution of Hg in a Canadian lake core. Further, evidence[9] from areas where the discharge of Hg has occurred, but has been halted, suggests that there has been little movement of Hg within sediments over periods of 15 to

Table 1 Mercury Content of Core Samples

Depth in core (cm)	Date	Hg content (p.p.b.)	Group
5	1950	1,050	Group D; average 1,026 p.p.b.
10	1935	1,034	
15	1915	1,005	
20	1895	620	Group C; average 608 p.p.b.
24	1880	579	
26	1870	626	
30	1800	363	Group B; average 286 p.p.b.
34	1670	175	
40	1520	331	
44	1400	280	
50	1260	152	Group A; average 122 p.p.b.
60	1020	95	
70	750	90	
74	660	168	
78	520	105	

45 yr. But the possibility of post-depositional movement of Hg within a sediment profile cannot be wholly excluded.

The vertical distribution of Hg could result from an increasing supply of Hg over the past half millenium, probably due to an enhanced release of Hg by man's activities. These include: denudation of land surfaces; heavy industry, mining and quarrying; burning of fossil fuels; and sewage disposal. Much of the Hg thus released initially enters the atmosphere, although some is introduced directly into natural waters. We suggest that the Hg contents of the core reflect, at least in part, this input by man. The sediments of Group A (Table 1) have an average Hg content of 122 p.p.b. which probably represents the local "background". Since ~1400 AD there has been a stepwise increase in Hg contents of the sediments which may correlate with man's activities, for example the change from Group B to C may reflect the onset of the Industrial Revolution. Pennington[7] suggests that the change from the brown clay to the black *Asterionella* ooze was caused by an increase in dissolved salts due to sewage pollution following human settlement on the lake shore. It is likely that the introduction of sewage in recent years will have resulted in an increased supply of Hg in the lake[8]. The combination of various factors comprising technological growth has, therefore, resulted in a progressive increase of Hg in the sediments of Lake Windermere.

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BIOLOGICAL SCIENCES

Molecular Model for Phase Transition in Biological Membranes

STUDY of phase transition of lipid molecules in biological membranes has been stimulated by the possible significance of this transition for membrane function, particularly for diffusion across the membrane. Here I propose for the first time a simple molecular field model which provides a quantitative measure of the ordering of membrane lipids as a function of temperature. It is based on theories which describe ordering in thermotropic liquid crystals, as described by McMillan[1].

In bimolecular lipid layers of artificial and natural membranes, the basic units are not rigid molecules as in classical liquid crystals but elements of hydrocarbon chains. The orientation of single elements in these is restricted because the valence bond angle remains constant and only a fixed number of *gauche* configurations of the molecule form energetically accessible states. Such a chain is statistically equivalent to a chain composed of a smaller number of elements with no restrictions to the possible orientations[2]. Here I shall treat the hydrocarbon chain of the lipid molecule as consisting of a number of segments which can assume arbitrary orientation. The number of independent segments for a given molecule is determined by comparison with the experiment described below.

The dispersive or Van der Waals forces lead to an anisotropic interaction of chain segments. This interaction can be described by the liquid crystal model of Maier and Saupe

$$V_{12} = -\frac{V_0}{N}\left(\frac{3}{2}\cos^2\theta_{12} - \frac{1}{2}\right)$$

where θ_{12} is the angle between the long axes and N the density of the molecules. In the molecular field approximation, this interaction leads to the one-particle potential in the molecular field η:

$$V_1(\eta) = -V_0\left(\frac{3}{2}\cos^2\theta - \frac{1}{2}\right)\eta$$

$$\eta = \left\langle \frac{3}{2}\cos^2\theta - \frac{1}{2}\right\rangle$$

where θ is the angle between the long axis of the segment and the preferred axis of orientation.

Further terms in the one-particle potential derive from other factors influencing the molecular order. In natural membranes, molecules packed between the hydrocarbon chains act to restrict the freedom of orientation and impose a degree of order on the chains. Cholesterol molecules[3] within the bilayer, for example, impose order on the neighbouring hydrocarbon chains and at higher concentrations prevent the transition to the disordered phase. The *gauche* configurations where the chain is bent at one or several places have energy higher than the *trans*-configuration. Near the planes defined by the polar heads, the chains cannot have a random configuration for purely geometrical reasons. Finally, the degree of smectic order influences the orientational ordering[1].

I propose to describe the ordering effect of all these factors by a single parameter, η_0, to be added to the molecular field. The one-particle potential becomes

$$V_1(\eta,\eta_0) = -V_0\left(\frac{3}{2}\cos^2\theta - \frac{1}{2}\right)(\eta+\eta_0)$$

In principle, η_0 is a function of the smectic order parameter which describes the tendency of polar heads to lie within the planes. However, as a first approximation, it can be assumed that the smectic order remains constant during the hydrocarbon chain transition and an η_0 independent of temperature can be

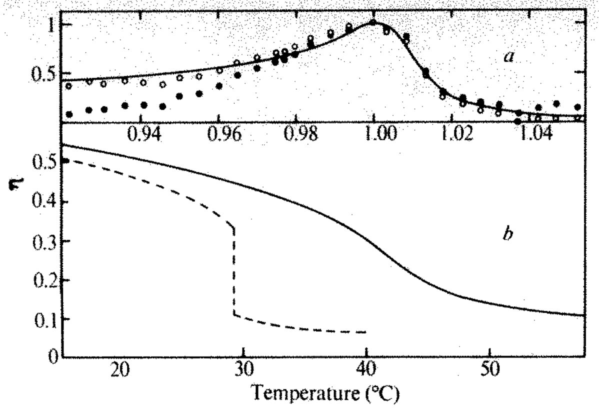

Fig. 1 (*a*) Specific heat of pronase-treated *M. laidlawii* membranes as a function of temperature. (——), Model result for $\eta_2=0.0174$; ●, data from ref. 4 with the baseline choice by the authors; ○, same data with the baseline determined by the least squares fit. (*b*) (——), order parameter for $\eta_0=0.0174$ corresponding to the specific heat data; (---), order parameter for $\eta_0=0.0070$.

used. This approximation is better for natural membranes where other molecules prevent large fluctuations in the position of polar heads (and thus increase the transition temperature slightly for hydrocarbon chains[4]). When the degree of smectic order is measured as a function of temperature (for example by X-ray scattering) the influence on the hydrocarbon chain order can be included in the model[1].

The order parameter η and other thermodynamic properties can now be calculated. The problem is formally equivalent to that of anisotropic molecules in an electric field discussed by Hanus[5], where the mathematical procedure is described. The equations for η and for the entropy are

$$\eta = \frac{\int_0^1 \mathrm{d}\cos\theta \left(\frac{3}{2}\cos^2\theta - \frac{1}{2}\right)\exp[V_1(\eta,\eta_0)/kT]}{\int_0^1 \mathrm{d}\cos\theta \exp[V_1(\eta,\eta_0)/kT]}$$

$$TS = -Nn\,V_0\,\eta^2 + NnkT\ln\int_0^1 \mathrm{d}\cos\theta \exp[V_1(\eta,\eta_0)/kT]$$

where n is the number of independent segments for the molecule. The specific heat is given by $C=T\,\partial S/\partial T$.

I have not included the effect of volume changes during the transition on the thermodynamic properties. Measurements from X-ray scattering on *Mycoplasma laidlawii* membranes by Wilkins, Blaurock and Engelman[6] show that the decrease in thickness of membrane during melting is compensated by the increase in membrane area, making the net volume change small.

Depending on the value of η_0, the present model predicts a continuous change of order with temperature or, for smaller values of η_0, a first-order phase transition[5]. The critical value of η_0 separating these two regions is $\eta_0=0.0103$.

Both these regimes have been observed experimentally. Natural membranes tend to show a continuous change of order, spread over larger temperature intervals if a significant fraction of cholesterol is present. Some of the artificial membranes which have more freedom for possible orientations of the hydrocarbon chain segments show clearly a first-order phase transition, such as those described by Krasne, Eisenman and Szabo[7].

I have compared the predictions of the present model with the calorimetric data on the phase transition in membranes of *Mycoplasma laidlawii*[4]. If the maximal specific heat and the corresponding temperature are C_M and T_M, respectively, a plot of C/C_M against T/T_M depends only on η_0, determined by a fit to the data. This is shown in Fig. 1 using specific heat data[4] on pronase-treated membranes of *M. laidlawii*.

The agreement between the model theory and the experiment depends also on the choice of the baseline for the specific heat anomaly data, that is, the choice of the boundary between the "anomaly" and the background. I believe that the method of Melchior *et al.*[4] is not necessarily the best as this method excludes the possibility of a term in the background which is linear in T. Such terms in the specific heat are generally present in complex systems. I have therefore shown the data with their baseline choice as well as with the baseline determined by the least-squares fit to the theory.

Using the value of $\eta_0=0.0174$ determined from the specific heat data, I have plotted the orientational order parameter η as a function of temperature for *M. laidlawii* membranes (Fig. 1*b*). The figure gives the average orientation of the hydrocarbon chain segments with respect to the preferred axis normal to the membrane plane. A solution for $\eta_0=0.0070$ corresponding to a first-order phase transition is also shown for comparison.

The average number of independent segments for membrane lipid molecules can be determined by comparing the experimental and the theoretical entropies. Transition entropy for the *M. laidlawii* membranes is typically[4] about 3.6×10^3 cal mol^{-1} corresponding to $n=7.7$ which is a reasonable value for a typical lipid molecule with 30 or 40 CH_2 units.

The large increase of the transition entropy with critical temperature[4] can be easily understood in the present model. As the length of the chains is increased the critical temperature rises[8]. The equivalent number of statistically independent segments is also increased in longer chains and hence the rise in transition entropy.

An independent test of the consistency of the present model is provided by the X-ray scattering data on *M. laidlawii* membranes[6]. The approximate change in the thickness of the membrane between 0° C and 40° C is 11 Å for erucate membranes and 8 Å for palmitate membranes. Assuming that $\cos\theta\sim\langle\cos^2\theta\rangle^{1/2}$ we can calculate the change in thickness of the hydrocarbon region upon warming. I do not have separate results for the order parameter in erucate and palmitate membranes, but from Fig. 1*b* it follows that, throughout the phase transition, η changes from about 0.55 to 0.15. Using these values, the corresponding changes in thickness are 8.9 Å and 7.1 Å for erucate and palmitate bilayer, respectively. I believe that the small difference between the measured and the calculated values is caused by the change in polar heads configuration during the transition.

Here, I have presented a simple model which provides a quantitative description of the ordering process in biological membranes, in agreement with the existing calorimetric and X-ray scattering data. This agreement will be further improved when the influence of positional ordering of polar heads and hydrocarbon chains is included in the calculation, resulting in a more realistic picture of this transition. Measurement of order parameters as a function of temperature would therefore be valuable.

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Short Term Heritable Changes affecting Viability in *Drosophila melanogaster*

Wild type chromosomes of *Drosophila* from natural populations, when tested for viability in homozygous condition, are generally found to consist of a mixture of lethal, semi-lethal and quasi-normal chromosomes[1]. Here we report an experiment carried out on semi-viable chromosomes to increase the viability by selection. We suggest that it is possible to modify the homozygote viability of some chromosomes, and that the modifications may be due to heritable changes in the chromosomes themselves, acquired over periods considerably shorter than normally expected for mutational changes.

The experiment was similar to that carried out by Dobzhansky and Spassky[2] in *Drosophila pseudoobscura*, except that the genetic background of *D. melanogaster* can be controlled to a greater extent, owing to the smaller number of major chromosomes and the greater availability of markers.

Second chromosomes of *D. melanogaster* were extracted from 20 wild type flies collected at five sites in the Hunter Valley district of New South Wales. These chromosomes were extracted and tested for viability in homozygous condition using the Curly/Plum method[1], modified slightly by outcrossing to ensure some variability in the genetic background[3]. Six of the original 20 chromosomes were chosen as having reduced viability (Table 1, column 2), and the remainder discarded.

Two replicate cultures were initiated from each of the six original lines using virgin wild type flies. These 12 cultures, each homozygous for chromosome II, were maintained in bottles for some 25 generations by tipping over large numbers of parents in each generation. These lines will be referred to as "homozygous lines".

At the same time two replicate cultures were started for each chromosome using virgin Cy/+ flies. The wild type chromosomes in these lines were maintained in heterozygous condition by using Cy/+ virgin flies as parents; all homozygous offspring were discarded. At least 20 pairs were used as parents in each generation of each line. These lines will be referred to as "heterozygous lines".

Homozygote viability was tested at two generation intervals until generation 14, and subsequently at generations 18 and 22.

Table 1 Homozygote Viabilities for Homozygous and Heterozygous Lines

Chromosome No.	Initial viability	Final viability Homozygous	Final viability Heterozygous
T1	0.91	0.91 0.87 (0.89)	0.93 0.83 (0.88)
T2	0.90	0.96 0.94 (0.95)	0.84 0.91 (0.88)
T3	0.64	0.83 0.92 (0.88)	0.54 0.57 (0.55)
T4	0.37	0.89 0.77 (0.83)	0.00 0.01 (0.01)
T5	0.33	0.46 0.60 (0.53)	0.27 0.13 (0.20)
T6	0.31	0.84 0.91 (0.88)	0.01 0.01 (0.01)

Average values for replicate lines are given in parentheses.

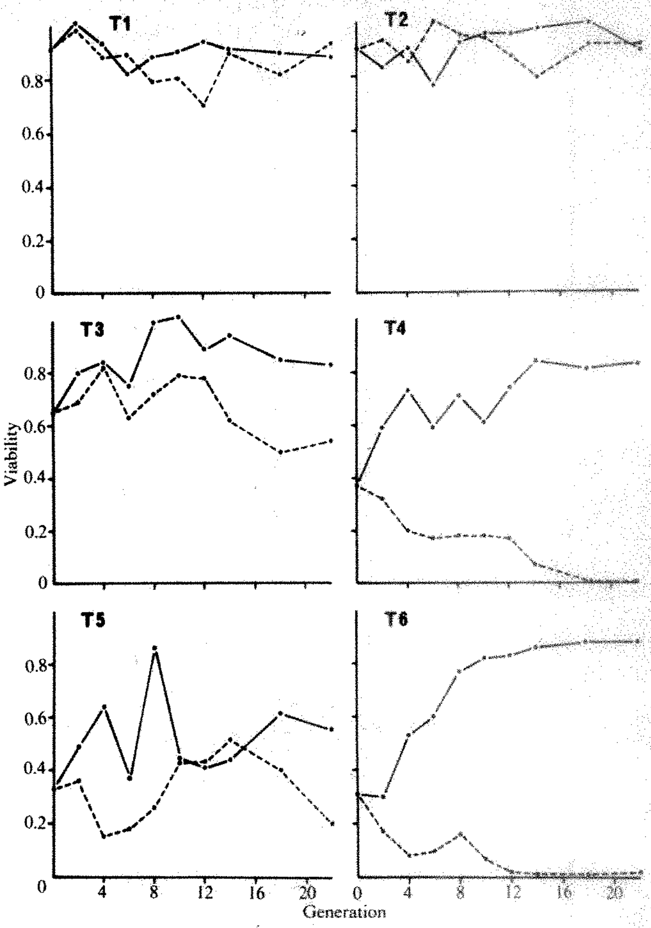

Fig. 1 Homozygote viabilities in homozygous (——) and heterozygous (- - -) lines from six original chromosome stocks.

In homozygous lines the Cy chromosome was introduced into each line by means of a Cy/Pm stock with genetically marked third chromosomes, including the Ubx inversion to prevent crossing over. Using the Cy/Pm stock as male parent, the Cy chromosome was introduced into the genetic background of each line, leaving only the Y chromosome and a proportion of chromosome IV uncontrolled. The equivalent test for the heterozygous lines was simpler, since Cy/+ stocks for the viability test were immediately available.

Viabilities over the course of the experiment are given separately for each chromosome in Fig. 1, in which results from replicate lines have been pooled. The viabilities attained in each line by the end of the experiment are also given in Table 1.

Chromosomes T1 and T2, those starting closest to normal viability, changed little in either homozygous or heterozygous lines. Marked changes were, however, produced in all other lines. In particular the viability rose in all cases in the homozygous lines, although considerably less in T5 than in the other lines. This rise was not unexpected, because continued use of homozygous flies as parents might have this effect under almost any selection hypothesis.

There was reduction in viability, however, in the heterozygous lines, most marked in T4 and T6 in which the homozygotes were essentially lethal by the end of the experiment. Because homozygote viability was tested and the chromosomes held as heterozygotes, the nature of the selective forces here was not clear. Competitive improvement in the heterozygote was considered but seemed unlikely, especially in view of the extreme reduction in homozygote fitness and the low conditions of competition under which the viability tests were carried out. Gametic selection was also ruled out, owing to the agreement with Mendelian expectations in all crosses between lines.

These results do not give any indication as to what extent

Table 2 Effect on Viability of Exchanging Genetic Backgrounds

	Chromosome II from Homozygous lines	Chromosome II from Heterozygous lines
Background unchanged *	0.85	0.01
Own background †	0.91	0.00
Replicate background ‡	0.84	0.02
Background exchanged §	0.84	0.01

* Viabilities within lines determined concurrently by the usual method.

† Control test of the crossing programme, chromosomes replaced in their original genetic background.

‡ Replacing genetic background with the background from replicate lines.

§ Exchanged genetic background between homozygous and heterozygous lines of the same chromosomal stock.

the changes in viability are due to changes in chromosome II, or to what extent they are due to genes on other chromosomes or cytoplasmic factors, referred to collectively as "genetic background". Conventionally, in the absence of any mutation, all of the effect must be attributable to changes in the genetic background and a crossing programme was carried out to test this. Using the genetically marked second and third chromosome stock mentioned above, it was possible in a six generation crossing programme to set up the cross Cy/+ × Cy/+, with the second chromosomes coming from one line and the genetic background from another. As before, only the Y chromosome and chromosome IV were uncontrolled. Chromosomes T4 and T6 only were used for this test, as the highest differences between homozygous and heterozygous lines were found for these chromosomes.

Results are summarized in Table 2; they have been combined for all four homozygous lines and all four heterozygote lines, because these were similar. The genetic background had very little effect on the viability, which appeared to be determined essentially by the constitution of the second chromosome.

These results are difficult to explain on a conventional genetic basis. The absence of any background effect is probably not by itself of any special significance. The changes which appear to have taken place in the homozygous chromosomes, however, could only be accounted for conventionally by mutation. This mutation would have to be very specific, and to occur at a very high rate. Also, the method by which the mutations spread at such a high rate through the heterozygote lines would require some special explanation.

Some further preliminary tests were carried out, primarily on chromosomes T4 and T6. First it was found that the high viability chromosomes are in all cases dominant, or nearly so, to the low viability chromosomes. Second, that high and low viability chromosomes could be re-extracted, apparently unaffected, from male flies produced by crosses between the homozygous and heterozygous lines. This procedure was also carried out for female F1 flies, in which recombination might be expected to have some effect, but the results in preliminary tests were not very different from the male results. Interpretation of these results is further complicated by the finding that chromosomes re-extracted from the high viability homozygote lines and tested individually appeared to consist of a mixture of high and low viability chromosomes.

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Histamine and Cyclic 3′,5′-AMP in Gastric Acid Secretion

IN slices from guinea-pig and rabbit cerebral cortex, histamine and a variety of compounds structurally related to histamine have been shown to enhance the formation of cyclic 3′,5′-AMP (adenosine 3′,5′-monophosphate)[1,2]. The order of potency of these agents was almost identical to their order of potency in stimulating gastric acid secretion[3], suggesting some similarity of receptor qualities both in cerebral cortex and in gastric mucosa, including the possibility that cyclic AMP might be an intermediate in histamine-stimulated gastric secretion.

Experiments were performed in SPF Wistar rats (180–200 g body weight). Subsequent to histamine diphosphate (HDP) application, the gastric acid output was determined using the perfused rat stomach preparation described in detail by Lai[4]. Gastric mucosal levels of cyclic AMP were measured by use of an isotope dilution procedure[5].

Fig. 1 shows dose-response curves to HDP given subcutaneously. The gastric acid output increased with increasing doses of the stimulant. Up to doses of 6 mg of HDP/kg rat body weight a fairly typical dose-response curve was obtained compatible with previous results[6,7]. The rise in acid secretion was paralleled by a dose-dependent increase in the cyclic AMP content of gastric mucosa. The correlation coefficient r satisfied the criteria for linear correlation between both the parameters ($r = 0.972$; $P < 0.01$).

To elicit temporal correlations between effects of HDP on gastric mucosal levels of cyclic AMP and on gastric acid secretion, 0.75 mg of HDP/kg rat body weight was injected rapidly into the femoral vein. Cyclic AMP contents almost doubled within 60 s, reaching near-maximal values, whereas acid secretion increased only after a lag period of 4 min (Fig. 2). This sequence of events adequately verifies one of the essential requirements set by Sutherland, Øye and Butcher[8] to determine whether cyclic AMP is or is not involved in a particular physiological process.

There is considerable evidence that histamine interacts with the membrane-bound adenyl cyclase system of parietal cells resulting in increased intracellular levels of cyclic AMP which as a second messenger takes over the role of histamine inside the cells. Certain xanthine derivatives known as inhibitors of the cyclic AMP degrading phosphodiesterase may potentiate the stimulatory effect of histamine on gastric acid secretion[9],

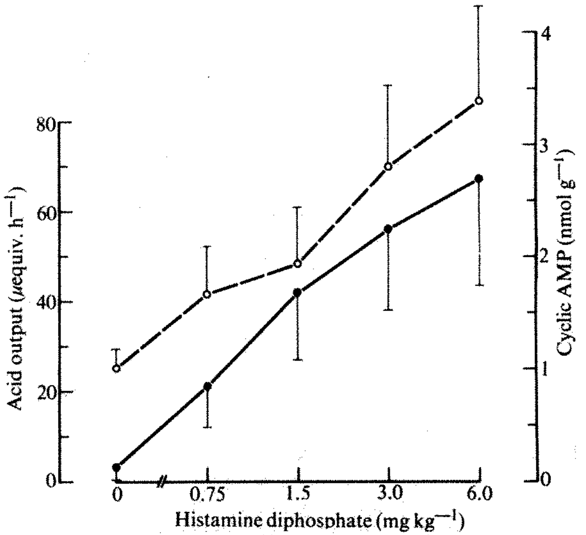

Fig. 1 Dose-response curves to histamine diphosphate given subcutaneously to rats. The scale for histamine dose is logarithmic. ○—○, Gastric acid output (μequiv. h^{-1}); ○ - - - ○, cyclic 3′,5′-AMP content of gastric mucosa (nmol/g wet weight). Each point represents the mean of determinations in 6 animals ± s.d. (vertical bars).

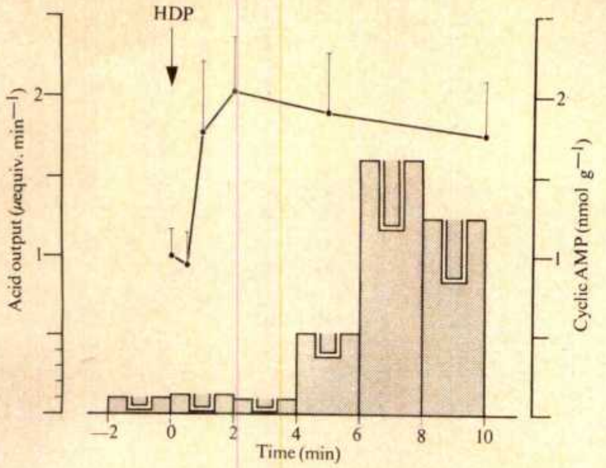

Fig. 2 Time-dependent effects of histamine diphosphate (HDP; 0.75 mg kg^{-1}) on gastric mucosal levels of cyclic 3′,5′-AMP (nmol g^{-1} wet weight) (○—○) and on gastric acid output rates (μequiv. min^{-1}; stippled blocks). Each point and block, respectively, represents the mean of determinations in 6 animals ±s.d. (vertical bars). HDP was administered to rats by rapid i.v. injection.

indicating adenyl cyclase as the most likely site of histamine attack. This was confirmed by Perrier and Laster[10] and by Nakajima *et al.*[11] who showed increased activities of the fundic adenyl cyclase due to histamine application both in guinea-pig and in *Necturus* gastric mucosa. In dogs, however, the situation appears considerably more complex, as the adenyl cyclase from canine gastric mucosa is not activated by histamine[12].

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Parallel Correction of Cancerous Growth and of a Genetic Defect of Cell-to-Cell Communication

THREE strains of cells have recently been found which, unlike normal cells, do not make junctions of a kind that connects the cell interiors to each other[1,2]. These three strains are also cancerous[1,2]. We explore here whether the junctional defect is related to the cancerous state of these cells; we fuse cells of one of the strains with normal cells that make junctions and examine the junctional permeability and growth properties of the resulting hybrids. This approach is based on the findings of Harris and Klein and colleagues, and of Weiss, Todaro and Green, that tumorigenicity is markedly reduced[3,4] and contact inhibition of growth resumed[5] in hybrids between various kinds of cancer and normal cells. This also turned out to be the case with the present cell systems. The question is then, is the normalization of the growth properties associated with normalization of junctional connexion? The results show that both defects are corrected in the hybrids.

Cells of four types were used: cells from a cancerous epithelial strain derived from a rat liver tumour (A strain[1]), cells from a normally growing (hereafter normal) fibroblastic strain derived from the same tumour (B strain[1]), a normal mutant of the B strain (see below), and cells from a normal liver epithelial line[2]. By use of the Sendai virus[6], the cancerous cells were fused with cells of each of the three normal types.

Junctional communication (coupling) was measured electrically and, simultaneously, by fluorescent tracer diffusion[1,7]. The measurements were done on multinucleate hybrids, the primary products of cell fusion (before they entered mitosis); or on their descendants in which the material of the parental nuclei had condensed into a single nucleus. The primary hybrids were easily distinguished from the parental cells during the measurements by the number of their nuclei; their hybrid nature was verified, after the measurements, by autoradiography (the nuclei of one of the parental cell partners were labelled with tritiated thymidine). The measurements on the mononucleate descendants of the primary hybrids were done on pure hybrid populations: (*i*) clonal populations of hybrids, each derived from a separate fusion between cancer cells and liver epithelial cells; or (*ii*) hybrids made with a thymidine kinase-deficient mutant selected from B cell cultures in media with progressively increasing concentration (up to 50 μg ml.$^{-1}$) of 5-bromodeoxyuridine[8]. To obtain pure hybrid populations of kind *ii*, we cultured the cells in medium containing hypoxanthine, aminopterin and thymidine (HAT)[9], in which the parental mutant cell cannot grow[10] (the cancerous parental cell and the hybrid, which both have thymidine kinase, grow in this medium); we then eliminated the cancerous parental cells and the fused cancer/cancer cells by repeated passaging in Dulbecco's medium[11], in which the two latter types do not adhere to the dishes[1]. (Aside from its usefulness for isolating a pure hybrid population, we worked with a B cell mutant here because the wild type tended rapidly to overgrow the hybrid; this was not quite so serious a problem with the liver epithelial cells.) We subsequently cloned the cells, so as to be able to measure coupling in populations the hybrid character of which had been established by karyotype. The karyotypes were examined on metaphase spreads of the clones treated with colcemid (0.2 μg ml.$^{-1}$, 3–5 h) after the coupling measurements. The modal number of chromosomes in the hybrids corresponded approximately to the sum of the modal numbers in the respective parental cells; moreover, the cancerous cell and the normal mutant parental cell had convenient marker chromosomes.

Tumorigenicity was tested with cell suspensions injected into the progeny of the Buffalo rats from which all parental cells had been derived. The suspensions contained normal and hybrid cells in the tests with primary hybrids, and only hybrids in the tests with later generations.

The cells were grown in plastic Petri dishes at 37° C; the cancerous parental cells in enriched F-12 medium[12] (the cells adhere to the dishes in this medium[1]), the normal parental cells in Dulbecco's medium, and the hybrids in either of these two media. The two media were supplemented with 10% foetal calf serum. The coupling measurements were taken at room temperature ranging from 23°–24° C and in a few cases at 37° C with the same results.

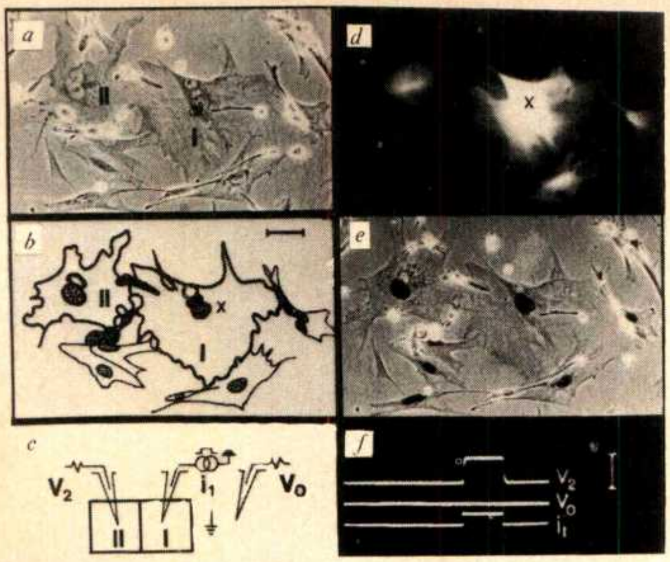

Fig. 1 Suppression of coupling defect by hybridization. Two hybrid cells (I and II) were produced by fusion of noncoupling cancer cells and coupling normal fibroblasts. The primary hybrids couple with each other and with normal fibroblasts from the parental strain. Hybrid *I* contains two normal fibroblast nuclei and one cancer cell nucleus. Hybrid *II* contains one nucleus from each parental cell. Coupling is probed electrically and with fluorescein 24 h after cell fusion. *a*, Phase contrast photomicrograph. *e*, Autoradiograph; the normal cell nuclei are ^{3}H-thymidine labelled. *b*, Tracing of the micrographs. *d*, Darkfield micrograph showing the results of fluorescein injection into hybrid *I*. Note that fluorescein has passed to hybrid *II* and to the adjacent normal parental cells, but not to the five parental cancer cells (the parental cancer cells are more refractile; hatched in *b*). Calibration, 50 µm. *f*, Records from an electrical measurement between two hybrids; *i*, current pulse (2×10^{-8} A, 100 ms duration) passed between interior of hybrid *I* and grounded exterior (*c*); V_2, V_0, the resulting voltage changes in hybrid *II* and in the exterior. Calibration 100 mV.

The parental cells were strikingly different in their growth properties. The A cell is noncoupling, its growth is not contact inhibited (it grows to densities of 10^6 cells cm^{-2} in culture) and it is highly tumorigenic (inocula of 10^2 cells produce fatal tumours in the animals). The three types of normal parental cells are coupled, contact inhibited (saturation densities $\leq 10^4$ cells/cm^2) and nontumorigenic[1]. The resulting hybrids took after their normal parents in all these respects.

Fig. 1 illustrates this for the coupling of the primary cancer cell/normal fibroblast hybrid. Two hybrid cells containing the nuclei of cancerous and normal (labelled) parents establish coupling with each other and with normal parental cells: fluorescein (330 MW) injected into one of the hybrid cells (*I*) is seen to have passed to a contiguous hybrid cell (*II*) and to four contiguous normal parental cells (there is no passage to any of the five contiguous cancerous parental cells); and a substantial fraction of the electric current injected into cell *I* is shown to have flowed through cell *II*. The junctional defect is evidently corrected in the hybrids. The example illustrated is typical of 11 cases examined. Similar results were obtained with the primary cancer cell/normal epithelial liver cell hybrids (14 cases) (Fig. 2).

The junctional defect was also corrected in the descendants of the primary hybrids. Eight clones of the cancer cell/normal (mutant) fibroblast hybrids and five clones of the cancer cell/liver epithelial cell hybrids were examined. Twenty-six coupling measurements were taken in which there was no cell membrane damage, as shown by measurement of input resistance[1] or by cellular fluorescein retention. In all these measurements the hybrids were found to be coupled to each other. (Each measurement was taken on a separate cell cluster where in each case coupling could be demonstrated by the fluorescein method for at least ten cell junctions and, in many measurements, for more than 20; Fig. 3.) The degree of electrical coupling between the hybrid cells and the extent of coupling, as seen by the fluorescein spread, were indistinguishable from those in the normal parental cells.

The correction is not simply due to cell cultivation or to cell fusion *per se*: the cancerous parental cells remain noncoupling (and tumorigenic) after many months in culture and, at least, the primary products of cancer/cancer cell fusion are noncoupling. The correction appears to be due to the normal cell genome in the hybrid.

The correction of the junctional defect was paralleled by a correction of the growth defect. The two types of hybrids were as sensitive to contact inhibition (saturation densities $\leq 10^4$ cells/cm^2; 3 clones of each hybrid type tested) as the normal parental cells and were not tumorigenic. With inocula of 10^6 cells, there was no tumour incidence with the primary hybrids (four animals injected) or their descendants (6 clones of each hybrid type tested; 12 animals injected) as against an incidence of 100% with the cancerous parental cells (36 animals). (Even inocula of 10^2 cancerous cells produced fatal tumours in four out of four animals. The incidence with the three types of normal parental cells was 0, fifteen animals.)

The results reveal a correlation between two phenotypic changes in the present cell systems: restoration of junctional coupling and restoration of normal growth. This encourages us in the idea that defective junctional coupling may be an

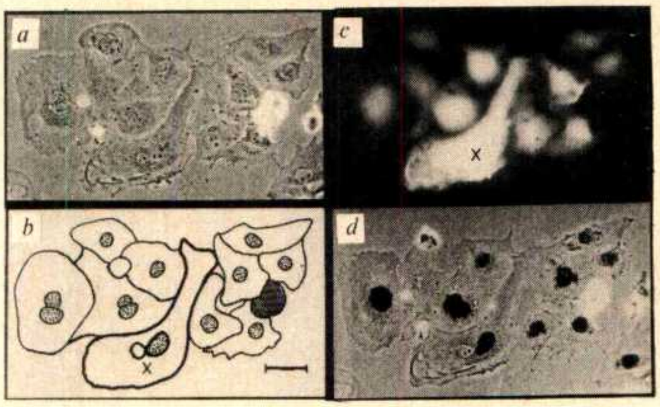

Fig. 2 A coupling primary cancer cell/normal epithelial cell hybrid. Fluorescein injection into the hybrid (×). Normal cell nuclei are ^{3}H-thymidine labelled (autoradiograph *d*). Parental cancer cell hatched in *b*. Calibration 50 µm.

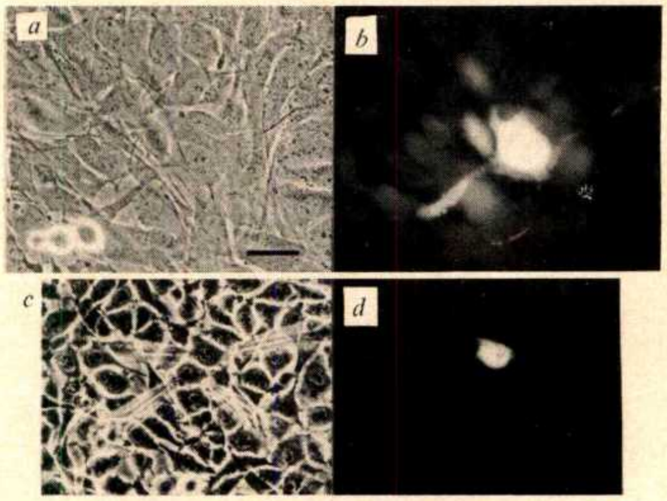

Fig. 3 Top row: coupling among cancer cell/normal (mutant) fibroblast hybrids. The cells are clonal descendants, of verified karyotypes, of the primary hybrids. The larger central cell with the long extensions was injected with fluorescein which, in *b*, is seen to have spread extensively through the clone. Bottom row: the noncoupling parental cancer cell. *b*, A fluorescein injection into a cell of a cluster of cancerous A′ cells. *a* and *c*, Photomicrographs in phase contrast; *b* and *d*, in darkfield. Calibration 50 µm.

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Influence of Cell-free Ascites Fluid and Adenosine 3′5′-Cyclic Monophosphate upon the Cell Kinetics of Ehrlich's Ascites Carcinoma

CELL and tissue growth regulation occurs in response to specific stimuli. Bullough[1,2] has shown that a number of tissues contain a saline-extractable, cell-specific substance, chalone, which can depress the mitotic activity of the corresponding cells in these tissues. He concluded that the presence of adrenaline and hydrocortisone was necessary in order to activate the chalone.

Increased and abnormal mitosis is a characteristic of many malignant cells and it has been suggested that this occurs because these cells lack the inhibitory influence of chalone, due to its leakage from the cells. In four transplanted tumours studied *in vitro* it was found that the addition of the appropriate chalone extract resulted in a reduction of mitotic activity as measured by the mitotic index (MI)[3,4]. Similar treatment *in vivo* caused regression of malignant melanoma in mice and hamsters[5].

Bichel[6,7] showed that cell-free fluid obtained from a mature mouse ascites tumour caused depression of MI when injected into a mouse bearing an immature tumour. He postulated that a growth regulating factor was present in ascitic fluid which appeared to produce similar effects to those of chalone.

attempting to characterize the chalone and determ relationship to cyclic AMP (P. R. C., in preparation). report preliminary results implicating cyclic AMP as a cell growth regulator.

The EAC tumour was maintained in this labora weekly intraperitoneal injection of 0.1 ml. of ascit containing 1×10^8 cells. Male mice, strain C3H, we throughout the investigation, and cells for injectic collected from mice bearing a 12 to 18 day old tumo cell-free chalone fluid was obtained by centrifugation o fluid from a mouse with a terminal tumour, that is, which the tumour was greater than 21 days old. It h found from *in vitro* experiments that the maximum to chalone in terms of MI to ascitic chalone occurr 14 day old tumour cells. In these experiments therefc bearing a 14 day old tumour were used.

The EAC cells were suspended in Hanks balanc solution containing 10% foetal calf serum so that cell count was 2 to 3×10^6 cells ml.$^{-1}$ of culture Ascites chalone fluid (0.2 ml. or 0.5 ml.) or cyclic AM or 100 µg) was added to tthe appropriate tubes. instances adrenaline 10 µg and hydrocortisone 10 µg d in 0.1 ml. balanced salt solution were added to the tum suspension. The final volume of culture medium wa and tumour cells were incubated in Leighton tubes for 4 h.

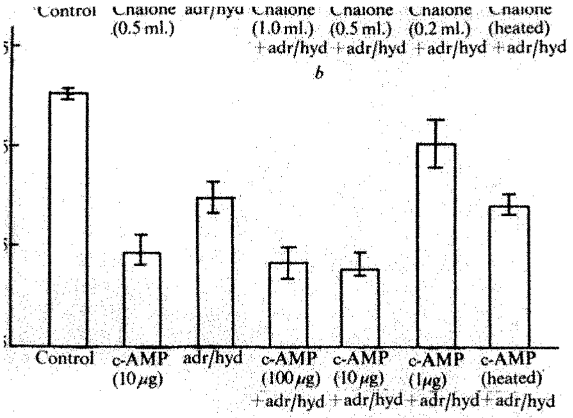
Colchicine, 10 µg, in 0.1 ml. balanced salt solution wa to each culture 3 h before harvesting to arrest the cells in metaphase; 1 h was allowed to elapse between of incubation and the addition of colchicine, so that already dividing could pass through metaphase.

Cells were harvested after 4 h incubation and proc display mitotic figures. The cells were swollen in hy medium (2 parts BSS : 8 parts distilled water) for then fixed in acetic alcohol (glacial acetic acid, 1 pa alcohol 95%, methyl alcohol 5%, 3 parts) for 20 mi pended in fresh fixative, spread on a microscope slide, dried for 30 min. The slides were then stained in 1% orcein for 30 min, dehydrated in alcohol, cleared i and mounted in DPX. The mitotic index (MI) was ca as the number of cells in mitosis per 1,000 cells. Appro 4,500 cells were counted per sample.

The *in vivo* experiments were also carried out usi bearing a 14 day old tumour. Chalone fluid was obtain terminal mice as described previously.

Animals were not given adrenaline and hydrocort these experiments as it was assumed these substance be available in physiological quantities in the intact Ascites chalone fluid 1.0 ml. and 0.5 ml., or cycl 50 mg kg^{-1} and 12.5 mg kg^{-1}, was injected 4 h before all injections were the same volume. Colchicine 20 to 25 was injected 3 h before sacrifice to arrest dividing metaphase. The cyclic AMP dose levels were determin preliminary experiments using a dose range of 25 µg 50 mg kg^{-1}. The cells were then processed as for the experiments and the MI calculated on the same basis.

Our experiments provided the following data: (cell-free ascitic fluid obtained from a terminal tumou did not inhibit EAC cell growth as measured by the index unless activated by adrenaline and hydrocortis

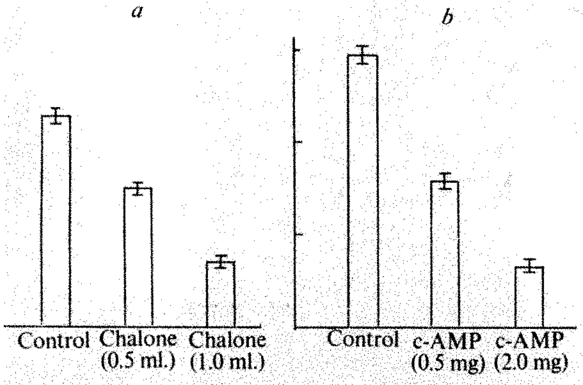


1 Effect of (*a*) added chalone and (*b*) 3′5′-cyclic AMP on EAC cells grown in cultures.

ed fluid produced a dose-dependent depression of mitotic (Fig. 1). Heating the chalone fluid to 100° C destroyed ıibitory effect. (2) The addition of cyclic AMP to EAC produced a marked depression of mitotic index (Fig. 1). chalone fluid, cyclic AMP did not require the presence ınaline and hydrocortisone to produce mitotic inhibition, ıe presence of adrenaline and hydrocortisone did not antly ($P>0.35$) increase the depression of mitotic index. e-dependent relationship was observed, there being a ant ($P>0.003$) difference between the depression of MI ed by 1 μg and 10 μg of cyclic AMP. Unlike chalone ıe mitotic inhibition produced by cyclic AMP was not antly ($P>0.1$) affected by heating to 100° C.

itro techniques can provide valid information on cell s in short-term experiments before the artificial growth n alters the tumour characteristics. The effect of bio-al change due to environment can be avoided if the r is studied *in vivo*.

experiments *in vivo* showed that both chalone fluid and AMP produced a significant depression of mitotic index 4 h period; chalone fluid (1.0 ml.) produced a 36.2% sion and cyclic AMP (50 mg kg^{-1}) a 47.1% depression). The response in both cases was dose dependent.



2 Effect of (*a*) chalone and (*b*) 3′5′-cyclic AMP on EAC cells *in vivo*.

both can be influenced by the same classes of drug and naturally occurring molecules[1,5] and both chalone and adenylate cyclase are cell-specific.

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Oestrogen Receptor Binding is not restricted to Target Nuclei

WHEN oestrogen molecules enter a target cell they are bound by specific receptors in the cytoplasm which then enter the nucleus carrying the hormone[1]. In the nucleus the hormone-receptor complexes bind to acceptor sites, where they presumably initiate the sequence of events comprising the hormone response.

Only target cells for oestrogen possess the specific oestrogen receptor[2-4]. There has been some suggestion that nuclear acceptor sites for oestrogen receptor are similarly only found in target cells[5-8], but there are other reports that oestrogen receptor binds equally in all nuclei[9]. We have determined quantitative receptor binding to nuclei prepared from several different tissues and have examined the recovered receptor by sucrose gradient sedimentation, and we find no significant difference in acceptor activity between target and non-target nuclei.

The cytoplasmic oestrogen receptor was prepared from rat uterus and charged with ^{3}H-oestradiol at 4° C before incubation at 25° C with crude nuclear pellets from various rat tissues (Fig. 1). Nuclear pellets from stomach, liver, or R3230AC mammary tumour retained as much receptor-bound oestradiol as nuclei from uterus, while spleen nuclei retained only a little less. Highly purified liver nuclei showed the same binding as the crude liver nuclear pellets. The R3230AC tumour, a transplantable rat mammary carcinoma which does not depend on oestrogen for growth, has only traces of receptor[10], though chromatin from this tumour is capable of extensive receptor binding[11,12]. Assuming about 6 pg DNA per diploid nucleus in the rat[13], all tissues tested bound at least 3,000–4,000 oestradiol molecules per nucleus.

To determine whether any qualitative differences appeared in receptor bound by target as opposed to non-target nuclei, we recovered the receptor from the nuclear pellets after cell-free incubation by extracting with 0.4 M KCl and applied the extracts to sucrose density gradients for centrifugation. Very similar sedimentation patterns were revealed in all cases (three are shown in Fig. 2). The 4–5S peak was identical to that seen for receptor from uterus nuclei after *in vivo* exposure to ^{3}H-oestradiol[14]. A 3S peak which was not seen *in vivo* appeared along with the 4–5S peak after the cell-free incubation. This 3S peak was found whether crude or purified nuclei were used, but not when receptor was incubated without nuclei.

To find the origin of the 3S peak, we used the discovery that receptor undergoes a temperature dependent transformation after binding oestradiol and before acting on th nucleus[15,16]. Cytoplasmic receptor charged at 4° C ca be transformed by warming to 25° C, especially in th absence of EDTA. When transformed receptor was incubated with nuclei at 4° C, the nuclei yielded a single 4–5S receptor peak like that found *in vivo* (Fig. 3). If untransformed receptor was used, however, only 3S receptor coul be recovered from the nuclei (Fig. 3). A similar observation has recently been reported[8]. We conclude that th 3S binding peak arises from nuclear binding of untransformed receptor under the artificial conditions of cell-fre incubation.

We therefore examined nuclei from uterus, spleen, liver stomach and R3230AC tumour after incubation at 4° C with transformed receptor. Similarly no difference in sedimentation between receptor from target and non-targe nuclei appeared (Fig. 4). Binding curves obtained with thi procedure were very similar to those already seen in Fig. 1.

These experiments reveal no differences between targe cells and non-target cells, either in the ability of their nucle to bind oestrogen receptor, or in the characteristics of th receptor after being released from binding. Publishe results for progesterone receptor binding to chromatin[7,17,1 and androgen receptor binding to whole nuclei[19] o chromatin[20] have suggested that more receptor is bound b target than non-target nuclear components in those systems but significant binding to non-target nuclei or chromatin i also seen. Even though we now question the evidenc that binding sites for oestrogen receptor are restricted t target tissue nuclei, the basic concept of steroid hormon initial action is essentially unchanged and the cytoplasmi receptor remains the primary determinant of tissu responsiveness. One might ask whether non-target nucle

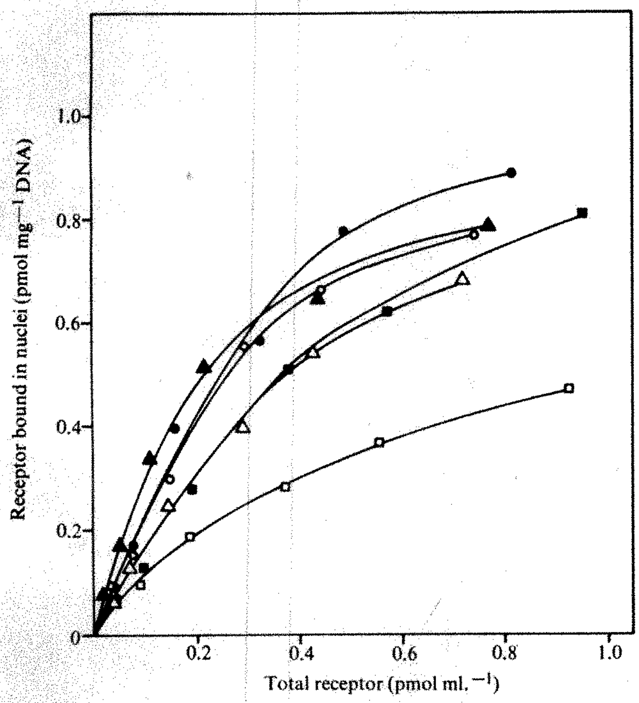

Fig. 1 Receptor bound to nuclei as a function of the total concentration of oestradiol-charged receptor (○, uterus nuclei; ●, R3230AC tumour nuclei; □, spleen nuclei; ■, stomach nuclei; △, liver nuclei; ▲, purified liver nuclei). Mature female Sprague-Dawley rats were killed 2–3 days after ovariectomy and tissues were homogenized at 4° C in 0.01 M Tris-HCl, *p*H 7.4, with 0.15 M KCl and 0.0015 M Na_2EDTA. Homogenates were centrifuged 40 min at 140,000*g*. The supernatant from uterus was charged with 1×10^{-9} M ^{3}H-oestradiol (95 Ci mmol^{-1}, New England Nuclear) for 1 h, and remaining free oestradiol was removed with dextran-coated charcoal[14]. Pellets from all tissues were washed by rehomogenizing in at least 10 volumes of the same buffer and recentrifuging. Pellets containing equal amounts of DNA (50–200 pg in different experiments) were homogenized in various amounts of the charged uterine supernatant which had been diluted to 0.5 ml. with the buffer, and were then incubated at 25° C for 15 min, chilled, diluted to 4.5 ml. with the buffer, and recentrifuged. Pellets were rehomogenized and aliquots were taken for determination of bound radioactivity and DNA. Purified liver nuclei were prepared by homogenization and 96,000*g* centrifugation in 2.2 M sucrose with 1 mM $MgCl_2$ and 0.1 mM Na_2EDTA. They were incubated with charged receptor as above and trapped and washed on 'Millipore' filters which were first placed in vials for radioactivity determination and then dried for DNA determination[21,22].

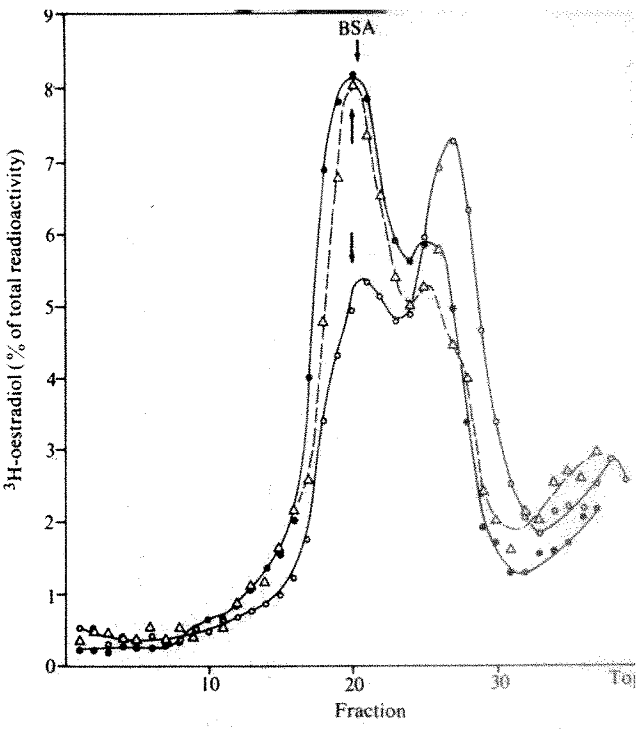

Fig. 2 Sucrose gradient sedimentation of receptor extracted from nuclei of several tissues after cell-free 25° C incubation with charged uterine receptor in Tris-EDTA, *p*H 7.4, 0.15 M KCl (●, uterus nuclei; ○, spleen nuclei; △, liver nuclei). Preparation and incubation followed Fig. 1 except for charging with 2×10^{-9} M ^{3}H-oestradiol and the use of 1 ml. undiluted cytosol and about four times the previous amount of nuclear sediment. Following incubation, pellets were homogenized in 0.4 ml. Tris-EDTA, *p*H 8.5, 0.4 M KCl. After 60 min the extraction mixtures were centrifuged at 140,000*g*, and 200 µl. of each supernatant was layered on 5–20% sucrose gradients in a 'Beckman SW 56' rotor and centrifuged 15.5 h at 308,000*g*. ^{14}C-Bovine serum albumin was included as a marker (arrow) in each gradient.

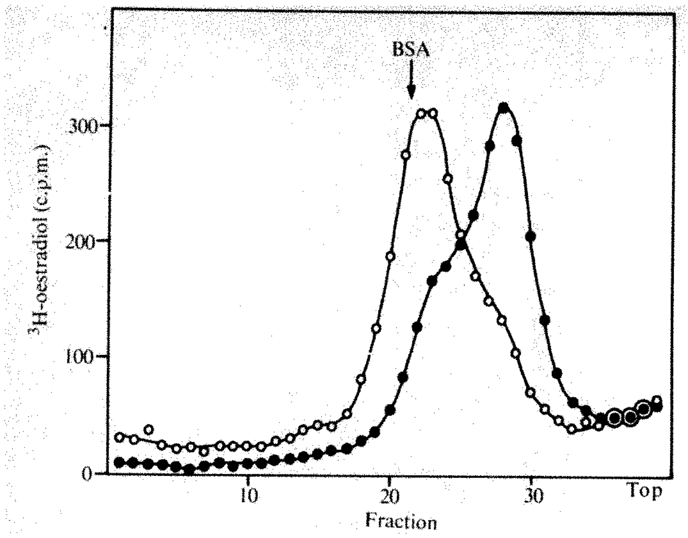

Fig. 3 Receptor extracted from uterus nuclei after incubation of nuclei at 4° C with transformed (○) or untransformed (●) cytoplasmic receptor in Tris-HCl, *p*H 7.4. Procedure followed Fig. 2 except for preparation and incubation in Tris-HCl, *p*H 7.4, incubation at 4° C for 60 min, and in one case warming of supernatant containing cytoplasmic receptor to 25° C for 30 min after charging at 4° C for 30 min.

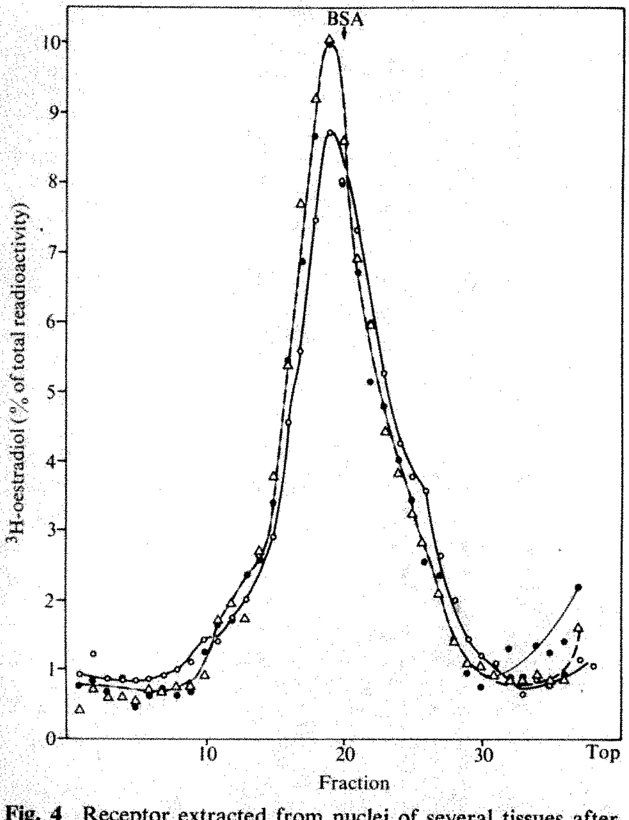

Fig. 4 Receptor extracted from nuclei of several tissues after incubation of nuclei at 4° C with transformed cytoplasmic receptor in Tris-HCl, *p*H 7.4 (●, uterus nuclei; ○, spleen nuclei; △, liver nuclei). Procedure followed Fig. 3, including warming of the cytoplasmic receptor.

could exhibit at least some of the characteristic responses to hormone if the receptor were provided. The experiments of Mohla *et al.*[16] show stimulation of RNA polymerase activity by charged oestrogen receptor in uterus nuclei but not liver or kidney nuclei, though polymerase activity is already much higher in the latter tissues than in unstimulated uterus. No other evidence is available at present.

High affinity binding of a receptor in the nucleus has not yet been proved to be directly involved in mediating the hormone response, nor has the specificity of the nuclear binding sites been rigorously demonstrated. It may be possible that other activities of the receptor in the nucleus or even in the cytoplasm, undetected by present techniques, have major roles in determining the response.

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Retardation of Foetal Growth and Plasma Protein Development in Foetuses from Mice injected with Coxsackie B3 Virus

Retarded intrauterine growth and low birth weight have been observed in association with congenital defects and foetal infection in humans[1-4] and, although animal model systems are available for the study of non-infective factors related to intrauterine growth retardation[5-7], the effect of pathogens on this aspect of impaired foetal development has not been the subject of much experimental investigation. Respiratory virus infection induced by parainfluenza 1 virus in rats causes foetal growth retardation owing to the maternal illness without

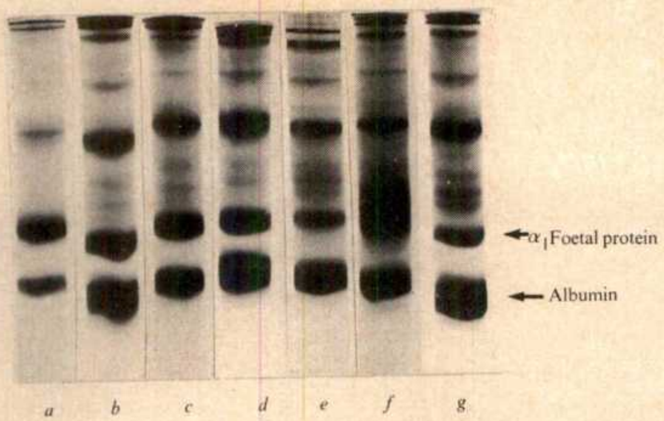

Fig. 1 Electrophoretic patterns of foetal and neonatal mouse sera. Disc gels of: *a*, 15 day foetus, control: non-infected; *b*, 18 day foetus, control: non-infected; *c*, 18 day foetus, infected: live virus; *d*, 18 day foetus, control: inactivated virus; *e*, 2 day neonate, control: non-infected; *f*, 2 day neonate, infected: live virus; *g*, 2 day neonate, control: inactivated virus. Electrophoretic conditions were: gels, 8% acrylamide containing 5% bisacrylamide; buffer, 0.037 M Tris/HCl of *p*H 8.6.

virus infection of the foetus[8]. The work described here, however, was carried out to study the effect of maternal infection on foetal growth and development with a virus previously shown to cause foetal infection in mice[9-11] without causing overt maternal illness.

Mice, eight days pregnant, were injected subcutaneously or i.p. with a dose of Coxsackie B3 virus between 10^5 and 10^6 tissue culture infective doses (TCD_{50}). Control animals were not treated or were given the same suspension of virus, inactivated by heating at 56° C for 30 min. The average weight of 142 foetuses, removed at 18 days gestation, from twenty-seven virus-treated mice was 0.952 g ± 0.057 g, compared with an average weight of 101 foetuses from fourteen control mice of 1.214 g ± 0.078 g. The difference between the two groups is highly significant ($P < 0.01$) and the maternal infection results in a reduction of foetal weights. During the experiments the pregnant mice remained in good health and did not appear to suffer any effects from the virus inoculations.

Serum levels of α-foetoprotein may be used as an indication of gestational age in human infants[12]. In the present experiments disc electrophoretic analysis of the plasma proteins revealed a low ratio of albumin/α-foetoprotein concentration in twenty-four out of thirty-four foetuses removed at 18 days gestation, compared with the ratio of these components in the plasma of foetuses from control mice (Fig. 1). It is also of interest to note that the ratio of albumin/α-foetoprotein concentration of the two day neonate from an infected animal is similar to that of a 15 day foetus from a non-infected animal, thus indicating that the maternal infection may have interfered with the development of the plasma proteins.

We therefore suggest that inapparent maternal infection during pregnancy may be one of the causes of retarded intrauterine growth and that a low ratio of albumin/α-foetoprotein concentration may be an indication of neonatal immaturity in animals and human infants.

We thank Mr M. J. R. Healy for the statistical examination of our results and Miss Heather La Roche and Mr Peter Carter for carrying out much of the technical work.

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clude, therefore, that ingested NTA does not increase toxicity or teratogenicity of ingested methylmercury hydroxide in rats.

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Hexosaminidase-A and Hexosaminidase-B: Studies in Tay-Sachs' and Sandhoff's Disease

HUMAN tissues contain two isozymes of β-D-N-acetyl-hexosaminidase[1]. Hexosaminidase-A (hex-A) is thermolabile and moves toward the anode on electrophoresis at *p*H 6.0, and hexosaminidase-B (hex-B) is relatively thermostable and moves toward the cathode. In Tay-Sachs' disease, which is found predominantly in Jewish populations, hex-A is absent but hex-B activity is increased[2-5]. In Sandhoff's disease, a variant of Tay-Sachs' disease, found mostly in non-Jewish populations, both enzyme activities are missing[3,6]. Thus, while it is apparent that there is a genetic relationship between hex-A and hex-B, the nature of this relationship has remained obscure. It has been suggested that hex-A may be derived from hex-B by the addition of neuraminic acid residues[1,7].

We have now purified human placental hex-B to homogeneity and hex-A to a very high state of purity. Antibody production against hex-A and hex-B has made possible further knowledge of the relationship between these two enzymes and the diseases which occur in their absence. Our studies of the purified enzymes and the antibodies produced against them resulted in the following three findings, which must be taken into account in any genetic and biochemical model explaining the relationship between these disorders.

First, although incubating purified hex-A with *Clostridium perfringens* neuraminidase at 37° resulted in the formation of a new, thermostable band resembling hex-B in electrophoretic mobility, the same band was also formed at the same rate in the absence of neuraminidase. Either in the absence or presence of neuraminidase only 5 or 6% of hex-A was converted to the more cathodic enzyme.

Second, as previously reported[8,9], antiserum produced against hex-B reacted with both hex-B and hex-A. Similarly, antibody produced against hex-A reacted with both hex-B and hex-A. We have made a specific anti-hex-A antiserum by treating serum produced against hex-A with purified hex-B. The converse, however, is not true. Treatment of anti-hex-B serum with hex-A resulted in absorption of all antibody activity.

Third, immunoelectrophoresis against anti-hex-B (which reacts both against hex-A and hex-B) gave two distinct arcs with normal liver and with liver from a patient with Sandhoff's disease. These arcs corresponded to the position of hex-A and hex-B activity. Only one arc corresponding to hex-B was found with liver from two patients with Tay-Sachs' disease. After elution of non-precipitated proteins from the phoresis slides, the arcs formed with norm purified enzymes stain for hexosaminidase 4-methylumbelliferone-β-D-N-acetyl-glucosami Tay-Sachs' liver, the single hex-B arc also zyme activity, but the arcs formed against hoff's disease were, of course, devoid of en

Table 1 Immunoelectrophoresis of Hexosaminida Normal, Tay-Sachs' and Sandhoff's Disease Li

Liver sample	Before treatment with antiserum		After treatment and el	
	Enzyme activity corresponding to mobility of:		Arc corresponding to mobility of:	
	Hex-A	Hex-B	Hex-A	Hex-B
Normal	+	+	+	+
Tay-Sachs'	0	+	0	+
Sandhoff's	0	0	+	+

Our findings are compatible with several seems unlikely that hex-B is merely the aneura of hex-A. It seems more probable that hex-A a common subunit. Sandhoff's disease would mutation of the active site of the common s Sachs' disease from a mutation affecting a sub in hex-A. Thus, hex-A may contain two d $(\alpha\beta)_n$ while hex-B has only one of these subu would explain the cross reactivity of anti against these two forms of enzyme, and the fa anti-A serum but not a specific anti-B serum c It also explains the increased amount of hex- in Tay-Sachs' disease, since uncombined β su available.

Details of these studies will be published els

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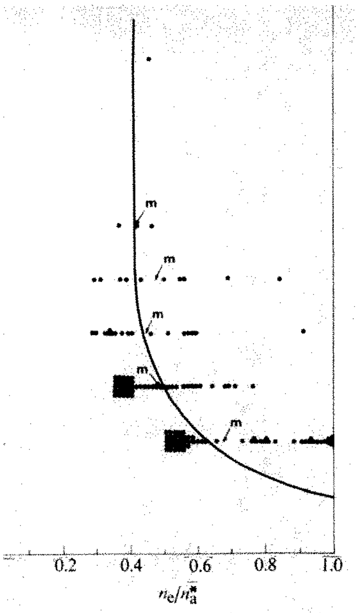
Another View of Neutral Al Natural Populations

JOHNSON[1] has suggested that the relationship the actual and effective numbers of alleles i populations is not consistent with the selectiv model of Kimura and Crow[2]. We show he the data from a large number of natural popul compatible with this model.

If *N* is the effective size of a population, *u* tion rate at a locus, n_a the actual number of a



ical curve for n_a^* versus n_e/n_a^*, and calculated
tural populations. n_a^*, Number of alleles with
)1; n_e, 1/(sum of squares of allele frequencies);
of n_e/n_a^* for each value of n_a^*. A point on the
represents data from one locus in one species.
listoni[3]—22 loci; *D. simulans*[4]—10 loci (*D.*
jected because two populations were not com-
inis and *D. athabasca* samples too small); *D.*
semispecies treated separately—up to 10 loci
29 loci in all; *D. obscura*[6]—14 loci; *D. ananas-*
D. pseudoobscura[8]—11 loci; *Peromyscus polio-*
Mus musculus musculus[10] (Denmark)—6 loci;
revirostris[11] (California)—11 loci; *Mus muscu-*
n Island)—*Pep-C* locus only; *Astyanax mexi-*
i; *Phasianus colchicus*[14]—*Tf* locus; *Limulus*
9 loci; *Clethrionomys gapperi athabascae*[16]—
Tf and *Al* loci.

tive number of alleles, then the relationship
n_a used by Johnson[1] applies when poly-
the same value of $4Nu$ are studied. If, how-
in a population are considered, it is highly
mutation rates will be the same at all loci, if
variation in the numbers of nucleotides per
opulations will differ in effective population
will vary when data from different loci in one
tions are used, and this must be taken into
tual data are compared with the predictions of

ple is drawn from a population the actual
ent alleles in the sample will be less than that
n, because rare alleles will tend to be missed.
tive number of alleles is little modified by the
ence of rare alleles, the ratio of the effective
ctual number of alleles observed in a sample
han that in the population. This bias is in-
alleles with frequencies of 0.01 or greater are

e consider only the actual number of alleles
of 0.01 or greater (n_a^*), then from Kimura and
opriate formula for the expected value of n_a^* is

$$^{*}_{a} = 4Nu \int_{0\cdot01}^{1\cdot0} (1-x)^{4Nu-1} x^{-1} \mathrm{d}x$$

ation, and the relation[2] $n_e = 1 + 4Nu$, the values
n be calculated for a range of values of $4Nu$.
lationship between n_a^* and n_e/n_a^* shown by the
Data from natural populations can then be
is relation.
comparison were obtained from a number of
ject to the following restrictions: (*a*) allele

more than 100 genes were sampled per locus (actual samples ranged from 112 to 7,696 genes); (*c*) data from laboratory colonies more than six generations removed from the wild were rejected.

It is also necessary to place some restriction on the sampling unit used. Sets of data on a particular locus from two different (but not reproductively isolated) populations of a species cannot be regarded as independent, since there will generally be a high correlation between the gene frequencies in the two populations. We have adopted the procedure of pooling allele frequencies from all available samples in a clearly defined species, after weighting by sample size. Where there is evidence of a high level of reproductive isolation between two or more populations of the same species, however, these have been treated separately; for example, *Mus musculus musculus* from Denmark and *M. m. brevirostris* from California, and the four semispecies of *Drosophila paulistorum*.

The results from over 130 polymorphisms are presented in Fig. 1. The mean value of n_e/n_a^* is indicated for each value of n_a^*. A random sample of fifty-seven is presented from the large number of diallelic polymorphisms available.

There is a close correspondence between the observed means and the theoretical curve, suggesting that the data are not inconsistent with the neutral allele model. We do not attach much significance to the wide range of values of n_e/n_a^* since computer simulation of neutral alleles (G. C. K., unpublished data) gives similar results.

A model for mutually heterotic alleles in a finite population has also been put forward by Kimura and Crow[2]. Preliminary analysis of this simple model shows that although the relationship between n_e and n_a^* may be more complex than in the neutral allele model, nevertheless in some cases at least, the relationship between n_e and n_a^* may not differ greatly from that predicted for neutral alleles.

Pending further studies of other models, we therefore suggest that the relationship between n_e and n_a^* presented in Fig. 1 should not be used in attempts to discriminate between neutral polymorphisms and those undergoing selection.

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Isolation and Identification of the Causative Agent of "Red Disease" of Pike (*Esox lucius* L. 1766)

Red disease has been described as an acute disease of pike fry, with unknown aetiology, causing severe losses in Dutch pike culture[1]. Its name was derived from the haemorrhagic lesions in the trunk, usually situated above the pelvic fins, and visible as bilateral red swollen areas in the diseased fry. In a serious outbreak during the spring of 1972 at a hatchery near Lelystad, only 0.6% of about 1,850,000 cultured young pike reached a length of 4 to 5 cm and could be used for stocking inland fishing waters. About 86% of the total mortality rate was due to red disease. Healthy fry placed in the same tank as diseased fry became infected, and it was concluded that the disease could be transmitted through water. No evidence was obtained that the disease was caused by bacteria. Here we describe work which demonstrates that the disease is caused by a rhabdovirus.

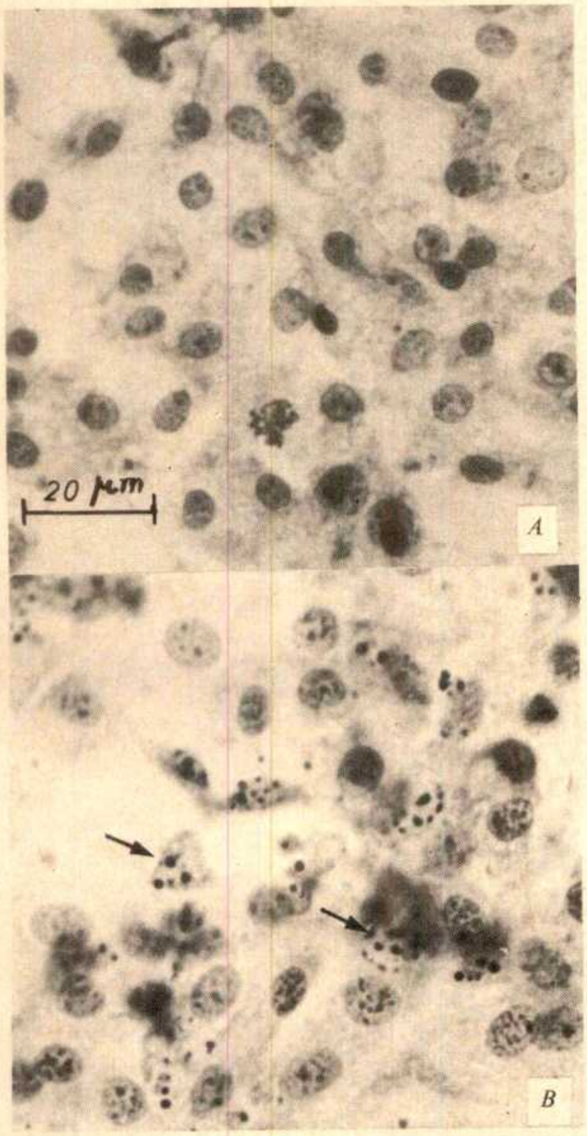

Fig. 1 CPE on FHM cells. *A*, Uninfected cells; *B*, cell changes 2 days post infection by 1 : 500 diluted filtrate from naturally diseased fries. Arrows indicate the granular degeneration of infected cells which precedes the destruction of the cell sheet.

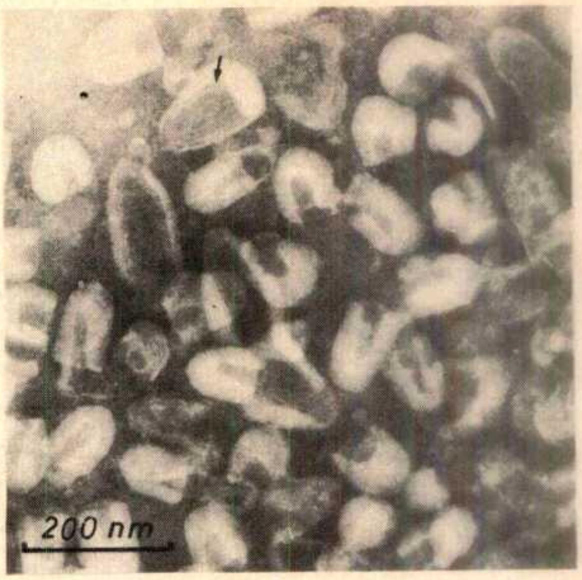

Fig. 2 Bullet-shaped viral particles from the second passage on FHM. The striations are distinguishable (arrow).

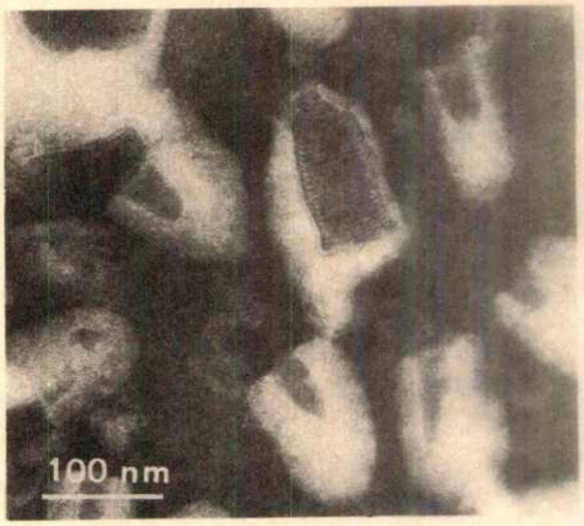

Fig. 3 Higher magnification view of one of the virus particles.

Diseased living fry showing characteristic haemorrhagic lesions were removed from the hatchery tanks, cooled in ice water, and transported to the laboratory. The fish were then packed in aluminum foil, frozen in liquid nitrogen, and stored in a refrigerator at −80° C. About two months later the frozen material was again placed into liquid nitrogen, and transported to France.

Ten frozen fishes were thawed in Earle's solution, with Tris buffer at *p*H 7.6. After complete thawing, the liquid was removed and samples were ground in a mortar and diluted 1 : 50 in cold Earle's solution. The suspension was centrifuged at 4,000*g* for 15 min and the supernatant filtered through a 450 nm 'Millipore' filter. The filtrate was used for infecting healthy pike fry and fat-head minnow cells[2]. The cells, grown in Leighton tubes, were infected with virus and, after 30 min adsorption, washed and 1.5 ml. of Eagle's medium (without serum but supplemented with the antibiotics penicillin, streptomycin and kanamycin) then added. The tubes were incubated at +14° C and checked daily for cytopathic effect (CPE) by comparison with control cells.

Strong CPE, involving cell rounding and monolayer destruction, resulted within 40 h (Fig. 1). Infection with ten-fold dilutions allowed us to observe the evolution of the CPE which was similar to that described for spring viraemia of carp (SVC) virus[3].

Electron microscopy of phosphotungstic acid stained pellets from the second passage in FHM cells established the presence of numerous bullet-shaped virus particles (Fig. 2) with one hemispherical and one planar end and an axial channel, partially penetrated by the stain. An envelope with projections

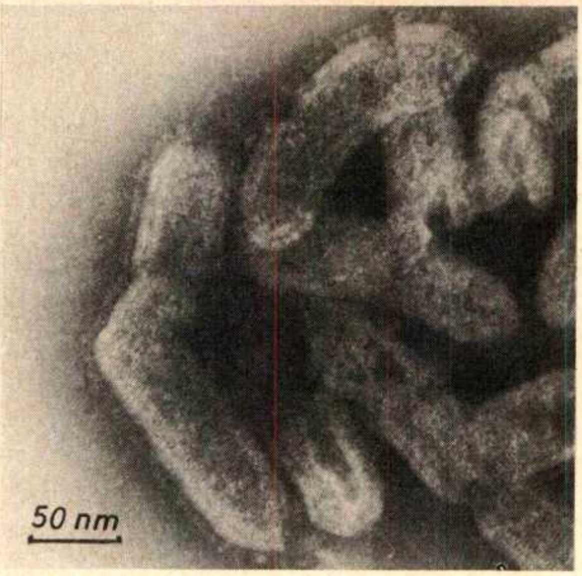

Fig. 4 Transverse striations and external projections observed on long forms of viral particles.

surrounded transverse striations running along the cylinder (Figs. 3 and 4). Dimensions were: length 125 ± 10 nm, overall diameter 80 ± 8 nm, channel diameter 25 ± 5 nm, and projection length 9 ± 2 nm.

Evidence that the disease was caused by an infectious agent was provided by intraperitoneal inoculation of four groups of young pike with (1) the initial isolate, (2) and (3) the supernatant from the second passage in FHM cells, (4) SVC virus. Control groups were inoculated with Eagle's medium. The different groups were checked for mortality, external lesions, virus isolation and histopathological changes. Moribund fishes were fixed in Bouin's solution for three days, embedded in paraffin and stained with haematoxylin–eosin. The results of this experiment are summarized in Table 1 and the mortality curves are given in Fig. 5. Only the infected fishes died, while those of the control groups remained healthy. Virus was recovered only from diseased pike.

Histological examination from groups 1 and 4 revealed lesions identical with those described in hydrocephalus and red disease of pike fry[1], tubular degeneration and necrosis of the kidney and haemorrhages in the connective tissue of the muscles. These lesions were less acute in the group infected with SVC virus.

The samples from the Netherlands used for the first isolation and transmission experiment had a titre of virus averaging 10^7 plaque forming units (p.f.u.) per 0.1 g of body weight of fish. The virus was re-isolated only from the experimentally infected fishes of the first and second groups; the other two were untested but most of the fries exhibited the macroscopic haemorrhages found in the natural disease. The experimental and natural infections produced the same histological lesions. The variations observed in the mortality rates could be due to the viral input; 10^6 p.f.u. per fish were inoculated in the first experiment and 1.2×10^7 in the second and third. In the latter case, the work was carried out at a water temperature ranging between +21.5° C and +24° C, which could explain the differences observed in the course of the disease.

It is unlikely that intraperitoneal inoculation is the natural route of infection. Because pikes spawn in late winter, and we received the samples in June, we were not able to find small pike fry (2 cm long) to demonstrate transmission by the water route. The natural disease mainly attacks young fry and we were running the risk of failing in experimental transmission with larger fry as we do not yet know anything about the usual age of infection.

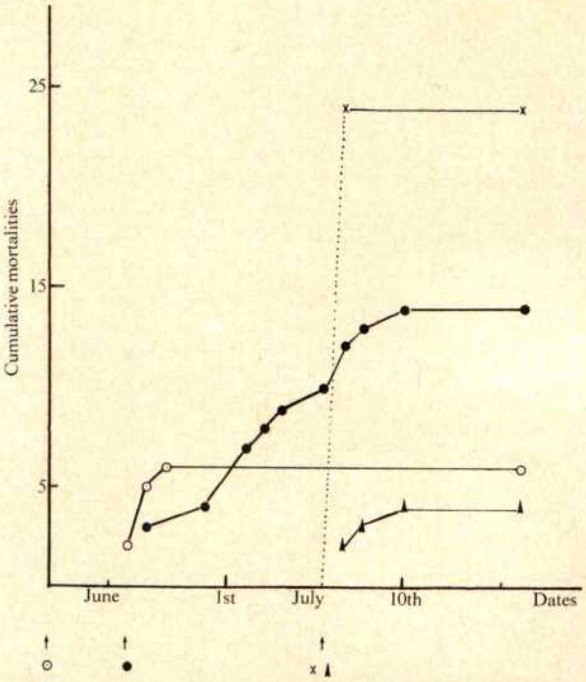

Fig. 5 Infection mortality curves. Arrows indicate the dates of inoculation. ○, First experimental group total fifteen fish; ●, second experimental group total fifteen fish; ×, third experimental group total twenty-five fish; ▲, fourth experimental group total seven fish.

In view of the knowledge of other fish diseases induced by rhabdoviruses, such as viral haemorrhagic septicaemia[4–6] (VHS), infectious haematopoietic necrosis[7] (IHN) of Salmonids or SVC[4], it seems likely that the pike virus is carried by adult fishes, spread into the water and, during the spawning time, onto the surface of the eggs, involving propagation of the disease very early in hatching time.

Morphologically, pike virus undoubtedly belongs to the rhabdovirus group, but it is still not known whether the virus is a new fish virus or a new serotype of SVC virus. It has the same shape, measurements, projections and transverse striations as SVC (ref. 3 and R. Scherrer, personal communication). We have also shown that the SVC virus infects pike and

Table 1 Summary of Experiments on Infection of Pike

No. of experiment*	Dose per fish (p.f.u.)	Water temperature (°C)	Size of fishes (cm)	Mortality		Virological checking	Pathological checking	
				Infected group	Control		Macroscopical lesions	Histological lesions
1	10^6	+14	5–6	6/15	0/15	+	+	+
2	1.2×10^7	+14	5–6	14/15	0/10	+	+	Not performed
3	1.2×10^7	+21–+24	6–1	24/25	1/25	Not performed	+	Not performed
4	4×10^7	+21–+24	6–1	4/7	0/7	Not performed	+	+

* Experiments 1 and 2 were carried out in France; experiments 3 and 4 were carried out in the Netherlands.

produces histological lesions of red disease but in a less acute form than pike virus. In FHM cells, both SVC and pike viruses induce the same CPE and their yields readily increase to high titres (2×10^8 p.f.u. ml.$^{-1}$) within 24 h at +20° C with an original virus input of 0.1 p.f.u. per cell. Although SVC virus antiserum did not neutralize the pike virus, it is possible that the two viruses are serologically distinct strains of the same virus.

The isolation of rhabdovirus from a pond fish other than carp is very important for fish pathologists. The role of viruses in the occurrence of acute red disease in ponds is still a controversial subject with numerous authors in Germany and Eastern Europe, even for SVC virus. The demonstration of the existence of another virus in pond fishes emphasizes that viruses could have a much more important role than previously envisaged in fish pathology. These observations will have to be taken into consideration in defining disease control measures in pond farming pathology.

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Environmental Modification of the Visual Cortex and the Neural Basis of Learning and Memory

IN the primary visual cortex of a normal cat the neurones are almost all orientation detectors, which respond only if an edge or bar at the appropriate angle moves across the receptive field: all orientations are equally represented[1]. But early experience can grossly modify the visual cortex. Blakemore and Cooper[2] reared two kittens in the dark except for a few hours each day spent in cylindrical chambers painted with black and white stripes at one orientation. These two animals, which experienced almost 300 h of exposure to stripes during their first 5 months of life, had no cortical neurones responding to the orientation perpendicular to the stripes that they saw when they were young. Almost all their cortical cells preferred orientations within 45 deg of the experienced angle. The phenomenon involves active modification of the receptive fields of the neurones, and not mere degeneration of unused cells, because there were no regions of silent cortex and no histological evidence of degeneration.

There is a brief sensitive period from about 3–14 weeks of age for this environmental modification, with particular sensitivity during the fourth and fifth weeks[3]. But in all these experiments the duration of exposure was typically about 30–50 h. One could argue that the whole paradigm is so unnatural that environmental modification can have nothing to do with the genesis of a functional visual cortex in a normal kitten, looking at a normal visual world.

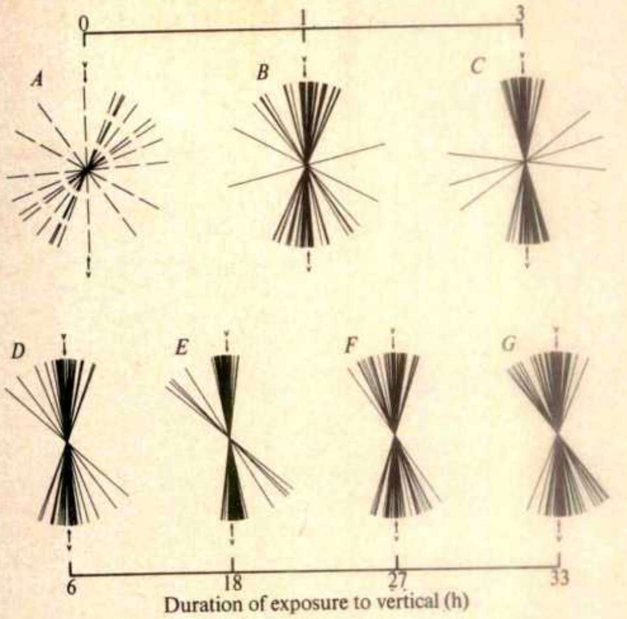

Fig. 1 Diagrams summarizing the effects on the visual cortex of different lengths of time spent in an environment of vertical stripes. Each line represents the optimal orientation for one cortical neurone: for the binocular deprived animal (*A*) the lines are interrupted to indicate that these neurones showed only the slightest preference for the angle shown and also responded to all other orientations. The number of hours of exposure for each kitten is indicated on the abscissae.

We now know that the process can occur in a very short time. We kept six kittens in the dark from before the time of natural eye-opening until they were about six weeks old, when we recorded from the visual cortex. During the recording the kitten was paralysed with an infusion of gallamine triethiodide and anaesthetized by artificial ventilation with a mixture of nitrous oxide and oxygen. We took the usual precautions to preserve good optical quality and plotted the receptive fields, through each eye in turn, by projecting moving or flashing spots, bars and edges on to a screen 57 cm in front of the kitten's eyes.

Table 1 Visual Experience of the Kittens

	Duration of exposure to vertical (h) at various ages													Total (h)
Age (days):	24	25	26	27	28	29	30	31	32	33	34	35	36	
B					1									1
C				1	1	1								3
D				2	2	2								6
E	2	2	2	2	2	2	2	2	2					18
F	3	3	3	3	3	3	3	3	3					27
G	3	3	3	2	3	3	3	2	2	2	3	2	2	33

A No patterned vision: binocularly deprived. 0

Knowing that the 28th day is a time of peak sensitivity, we exposed these six kittens in a vertically striped cylinder for totals of 1, 3, 6, 18, 27 and 33 h, on or around the 28th day (Table 1). This was the only vision they experienced, except for a few seconds of dim red light from a flashlight each day, during feeding and cleaning. A seventh kitten served as a control animal with no visual experience: both eyelids were sutured before natural eye-opening and the kitten was kept in a normal lighted room. We reopened the lids only just before recording from the cortex.

The polar diagrams of Fig. 1 show the results for all seven animals. In these plots each line is the preferred orientation for one neurone. The lines are shown interrupted for the zero-hour, binocularly-deprived kitten (Fig. 1*A*) because we were unable to find any neurone that had more than the vaguest orientational preference. In this animal there were large numbers of visually-unresponsive cells and cells with no orientational preference whatever. Even the neurones illustrated in Fig. 1*A* responded a little to all orientations and had only the slightest preference for the angles shown. Thus we find ourselves in agreement with Barlow and Pettigrew[4], who report this pattern as the typical organization of the visually inexperienced cortex, and somewhat at odds with Wiesel and Hubel[5], who maintain that many neurones in such an animal are wholly adult in their properties.

The visual cortex of even the kitten exposed for 1 h (Fig. 1*B*) was completely transformed: virtually every cell responded briskly over a narrow range of orientation and the distribution of preferred orientations was strongly biased towards vertical. The few cells maximally sensitive to other angles generally had more infantile properties, such as broad orientational tuning, sluggish responses and rapid habituation. We found them, along with a few non-oriented and visually unresponsive cells, in small regions between the totally normal columns of neurones preferring vertical or near-vertical edges.

For successively longer exposures (Fig. 1*C–G*) there was a further slight improvement in the narrowness of distribution of optimal orientations and a decreasing probability of finding any infantile neurones. But the difference between 0 and 1 h of vision was much more striking than the final refinements between 1 and 33 h.

The analogy between this process and the ill-understood basis of learning and memory is now no longer far-fetched. We have no idea what fundamental structural transformation in the brain is the physical manifestation of a memory, but it may be very similar or identical to environmental modification of cortical cells. If we can understand this relatively simple phenomenon, perhaps we shall be closer to solving the mystery of memory.

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Defects of Non-Verbal Auditory Perception in Children with Developmental Aphasia

SOME otherwise normal children fail to learn to speak and are designated developmental aphasics. Several authors have suggested that auditory perceptual deficits, particularly of sequencing, may be the primary dysfunction[1–4]. Efron[5] suggested that the left temporal lobe mediates temporal analysis and that it is the disruption of this function which is central to adult aphasia. We examined children with developmental aphasia and demonstrated inferior discrimination of sound quality to which a sequencing difficulty could be secondary.

The subjects were nine boys and three girls, aged 6.8 to 9.2 years, from the John Horniman School for Aphasic Children and twelve normal children matched for age, sex and non-verbal intelligence. The aphasics were free from other signs of neurological dysfunction, had normal hearing, and a mean non-verbal IQ of 108 (85–127).

Two different sounds were presented sequentially and subjects were examined for their ability to indicate (*a*) the order in which the sounds occurred or (*b*) whether the two sounds were the same or different. Stimuli were two 75 ms complex tones of frequencies within the speech range (fundamental frequency: Tone 1 = 54 Hz, Tone 2 = 180 Hz; rise/fall time 40 μs^{-1}). Normal speech rates approach 80 ms per phoneme. Stimuli were generated by a 'Speech Synthesizer' and 'Modular One' computer, recorded onto a 'Uher' tape recorder and played to subjects through earphones. Subjects responded on two identical depressible panels.

We used two test methods. In the repetition method subjects were trained to respond to each tone separately by pushing the left panel to Tone 1 and the right to Tone 2. Discrimination training continued until criterion was reached (20 of 24 consecutive responses correct, $P<0.001$ binomial test). Subjects were then trained to respond to each of the four possible two-tone sequences (1-1, 1-2, 2-1, 2-2) by pushing the panels in the corresponding order. The inter-sound-interval (ISI) was 428 ms. Correct responses were demonstrated four times by the experimenter followed by eight training trials in which subjects received knowledge of results and error correction. Next, 24 trials without knowledge of results were given. Subjects were then tested on a total of 48 two-tone sequences with ISIs of 8, 15, 30, 60, 150, 305, 947, 1,466, 1,985, 3,023, 3,543 and 4,062 ms, all presented in random order. A similar procedure was used with the same two tones for sequences of three and four elements (ISI 428 ms).

Because a subject may perceive the elements of a temporal sequence but not be able to reproduce a corresponding motor pattern, a same-different method was also used[6]. The response panel was turned through 90° to avoid confusion between methods. Subjects were initially presented with the two tones (ISI 428 ms) and trained to press the top panel if the tones were the same and the bottom panel if different. Training continued until the criterion described above was reached.

The same series of two-tone sequences, 24 with ISI 428 ms and 48 with ISI varied as above, were again presented and the subject indicated whether the two tones were the same or different. Half of the subjects in each group performed the repetition task first; half performed the same-different task first.

On the repetition task, all the aphasics and controls were able to reach criterion both on the initial auditory discrimination and on the reproduction of the two tones separated by 428 ms. However, when the interval between the two tones was decreased, the aphasics' performance was markedly impaired (Table 1). On the repetition test, whereas the controls as a group performed significantly better than chance ($P<0.001$) at the shortest ISI (8 ms), this level of performance was not achieved by the aphasics at ISIs less than 305 ms. By contrast, increasing the ISI had no adverse effect on aphasics' performance. They performed with undiminished efficiency ($P<0.001$) when the interval was increased up to 4 s. When the number of elements in the sequence was increased to three, only two of the aphasics reached criterion. All controls reached criterion on both three and four element sequences.

Results for the same-different task showed a similar pattern. Both groups performed accurately ($P<0.001$) at 428 ms ISI but, when the interval between tones was decreased, controls remained virtually errorless at all intervals whilst the aphasics again required at least 305 ms to perform at the level of accuracy defined above.

Correct performance on the same-different task requires discrimination of the two tones but not identification of the

Table 1 Judgment of Two-tone Sequences by Normal and Aphasic Children

Inter-stimulus Interval (ms)	Repetition method correct %		Same-different method correct %	
	Normal	Aphasic	Normal	Aphasic
8	87*	61	83*	71
15	94*	61	92*	71
30	92*	64	98*	65
60	93*	64	98*	63
150	92*	58	100*	71
305	100*	76*	100*	90*
428	100*	94*	100*	98*
947	100*	94*	100*	98*
1,466	100*	97*	100*	96*
1,985	100*	93*	98*	98*
3,023	100*	98*	98*	100*
3,543	100*	98*	100*	100*
4,062	100*	97*	100*	94*

*$P<0.001$ binomial test (66% for repetition method; 73% for same-different method).
Percentages are based on totalled scores for each group.

order in which they occur. The ISI at which the aphasics fail to reach the criterion of $P<0.001$ on a binomial test is the same for both the repetition method (which does require perception of order) and the same-different method (which does not). Accordingly, Efron's and Lowe and Campbell's observations that aphasics exhibit impairment of auditory perception of rapidly presented sequences may be explicable in terms of a failure of discrimination of auditory quality.

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Receptive Fields of the Visual System of the Squid

IN an octopus some second order visual cells that receive synapses in the plexiform layer from the optic nerve fibres have dendritic fields with an oval orientation lying in the horizontal plane[1]. It has now been shown that in a squid there are cells with several distinct types of receptive field, which are suitable to act as detectors of visual contours of differing size, shape and orientation. The largest have oval dendritic fields, several millimetres long, predominantly orientated along the vertical (dorso-ventral) axis of the optic lobe (Figs. 1 and 2). Each makes contact with the endings of many thousands of optic nerve fibres and therefore they are probably activated only by very large visual contours. Their large axons reach deep into the optic lobe, from which the axons of third order cells reach direct to the first order giant cells. This may therefore be the pathway for escape reactions from large objects, perhaps also for schooling responses to other squids. The cell bodies of these second order visual neurones lie at the base of the inner granule cell layer and their trunks bend over in the second tangential layer of the plexiform zone to make recurrent axons (Figs. 1 and 3).

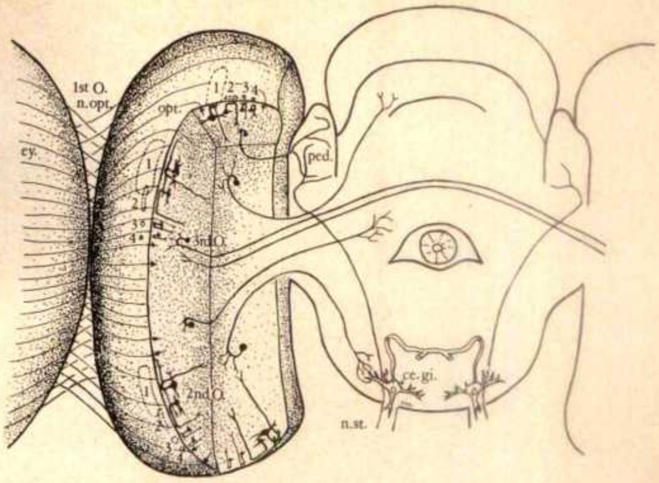


Fig. 1 Diagram of the four types of second order neurone seen in the optic lobe of *Loligo*. The fields of their dendrites are outlined on the surface and numbered 1–4 in decreasing order of size. Only a few further connexions are shown. ey., eye; ce. g., giant cell; opt., optic lobe; ped., peduncle lobe; n. st., static nerve; 1st O. n. opt., fibres of the optic nerves; 2nd and 3rd O., second and third order visual neurones; 1–4, receptive fields of the second order cells.

Much more numerous second order visual cells have long but very narrow dendritic fields in the first tangential plexiform layer. Their receptive dendrites are short collaterals spread along a single trunk (Figs. 4 and 5). The trunks proceed in various directions over the surface of the lobe, but most are orientated along the vertical axis. Each of these cells is presumably activated only by a narrow visual contour. The whole web of them provides a system capable of responding differentially to complex visual configurations. Numerous amacrine cells among the visual nerve endings provide possibilities of lateral interaction and inhibition (Fig. 4).

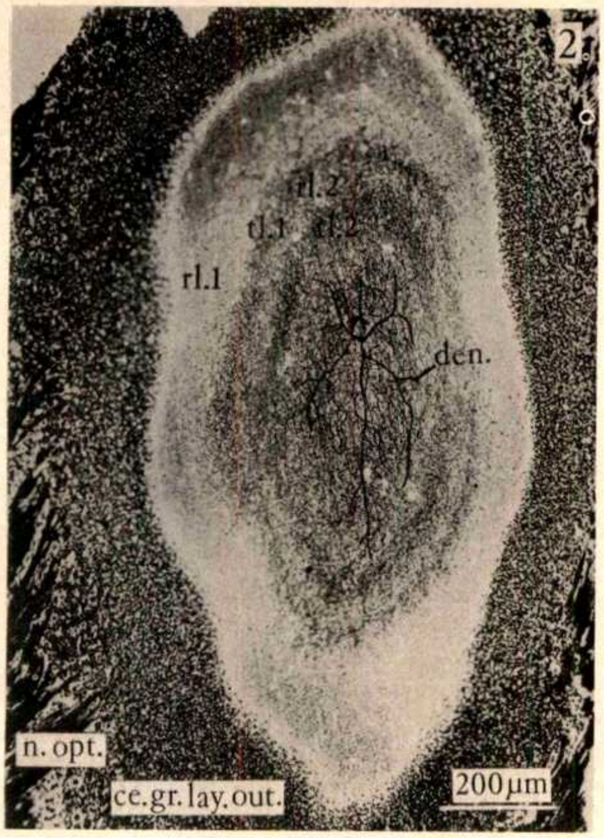
The neurones with elongated receptive fields also have their cell bodies in the inner granule cell layer and their axons turn down at the end of the elongated "dendritic" section (Figs. 4 and 5). They proceed to the more superficial levels of the optic lobe where they break up among the processes of numerous small multipolar cells (Fig. 5). This system presumably allows appropriate interactions between the activities of the second order visual cells and signals are passed on further into the lobe by third order cells (Fig. 1).

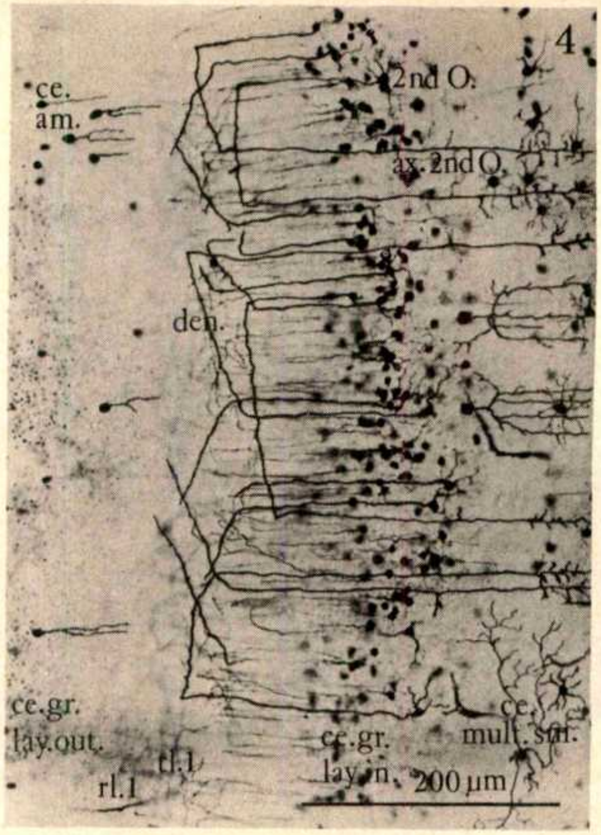
Besides the neurones with orientated receptive fields there are at least two sorts with circular dendritic fields of various sizes just above the first tangential layer (Figs. 5 and 6). They presumably have circular visual fields. The smallest are in contact with only a very small number of optic nerve fibres, perhaps each with only one; their axons turn inwards and break up near the surface of the lobe.

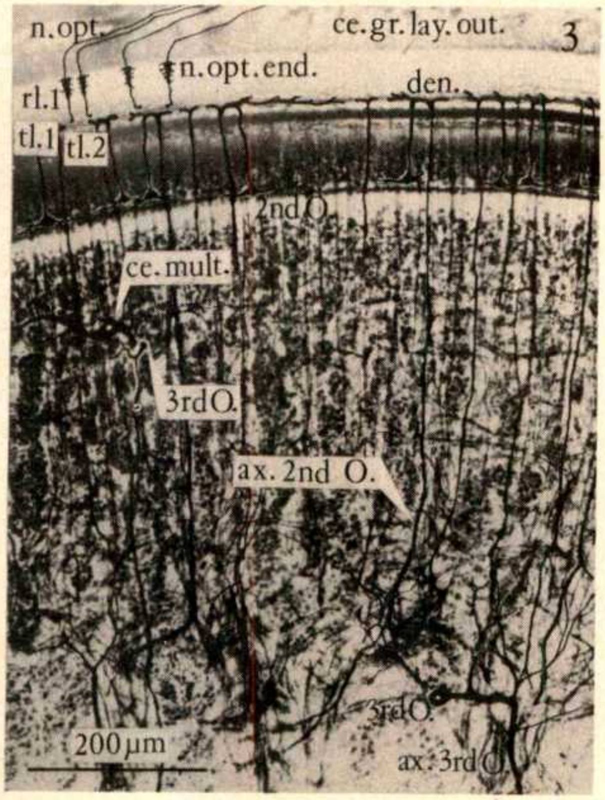
The possibility of identifying these various types of cell has depended on successful Golgi impregnation in squids. There is little doubt that similar types of cell exist in octopuses and cuttlefishes. The different types of receptive field are largely segregated in the different layers of the plexiform zone. This layering is similar in octopods and decapods, but the former lack the largest cells.

The analysis shows that the plexiform layer of cephalopods provides a system of feature detectors for classifying and encoding the visual input. The categories of visual field suggested by the various types of dendritic field have some obvious similarities with those found by Maturana *et al.*[2] in the frog or by Hubel and Wiesel[3] in the visual cortex of mammals. It will be interesting to discover whether such visual fields can be found experimentally in cephalopods.

At the stage beyond the plexiform zone the integration of







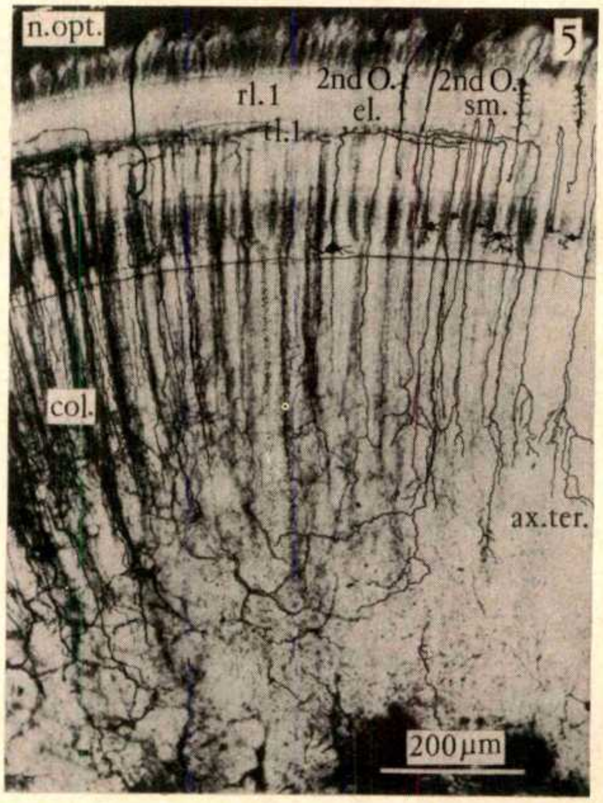


Fig. 2 Sagittal section tangential to the surface of the optic lobe, showing the various layers and the dendritic spread of one large second order visual neurone (den.). Cajal's stain. This and the following figures have been retouched. n. opt., optic nerves; ce. gr. lay. out., outer granule cell layer; rl. 1, rl. 2, radial and tl. 1, tl. 2, tangential layers of the plexiform zone.

Fig. 3 Transverse section to show the largest second order visual neurones, (2nd O.) and two third order cells (3rd O.). Cajal's stain. ce. mult., large multipolar horizontal cell; n. opt. end., optic nerve ending; ax. 2nd O., second order cell axon; ax. 3rd O., third order cell axon.

Fig. 4 Second order visual cells with long straight receptive fields (den.) at various orientations, with axons proceeding to the medulla. Also amacrine (ce. am.) and small multipolar cells (ce. mult. sm.) and inner granule cell layer (ce. gr. lay. in.). Golgi-Kopsch.

Fig. 5 Second order visual cells with long straight receptive fields (2nd O. el.) and others with very small fields (2nd O. sm.) at right. The axons form columns in the outer part of the medulla (col.) and terminate there. Golgi-Kopsch.

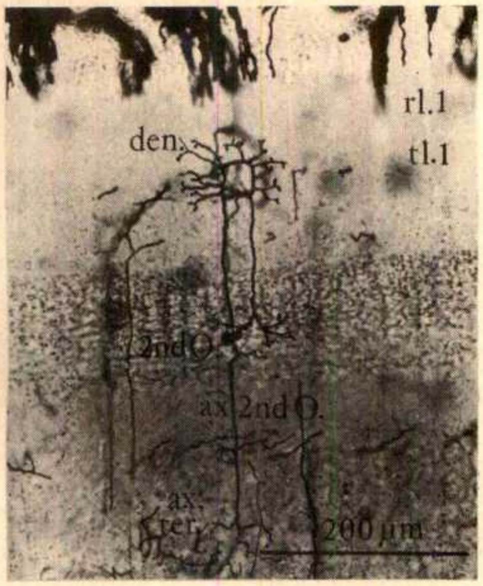


Fig. 6 Second order visual cell with a circular dendritic field lying in and above the first tangential layer. Golgi-Kopsch.

the actions of the various classifying cells is achieved by a system of columns linked by layers of tangentially spreading cells (Figs. 3 and 5). This must be the system by which selection is made of the response appropriate to each visual pattern. Signals are then sent on to the lobes of the central brain by visual neurones of a third or higher order. This system of columns has a certain similarity to the cerebral cortex of mammals, but its mode of functioning remains to be investigated.

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Anodic Oxidation of Urea and an Electrochemical Approach to De-ureation

ONE of the major functions of an artificial kidney is the removal and excretion of nitrogenous waste products. A newer type of artificial kidney (REDY)[1-3] converts the urea to ammonia by the action of encapsulated urease. For elimination, the toxic ammonia must then be adsorbed. This device uses a conventional type of dialyser with a recirculating regenerative dialysate system, which does not need large quantities of dialysis fluid. As the dialysis membrane will not filter bacteria, the system can be filled with a small volume of tap water. In practice, a multitude of unwanted waste materials are adsorbed on an activated carbon cartridge, and the urea is converted to ammonia which is then adsorbed on zirconium phosphate. The phosphate concentration of the dialysate is controlled with zirconium oxide; unfortunately the zirconium compounds are expensive, thus one of the major potential advantages of the system, low cost in use, is not achieved.

One approach to the artificial kidney could be the electrochemical degradation of the nitrogenous wastes and their conversion to non-toxic products, capable of excretion by other means. For example, if nitrogen containing wastes were converted to water, carbon dioxide and nitrogen, the water would be absorbed into the body water pool and the CO_2 and N_2 could be excreted by the lungs. An electrochemical device could conceivably oxidize many of the substances[4,5] which the kidney normally needs to handle, however, the amount of urea produced by the body requires that any artificial kidney be able to handle large amounts of this substance.

From experiments in this laboratory we conclude that urea may be oxidized electrochemically without prior enzymatic hydrolysis to NH_3 and CO_2. The end products could be N_2, CO_2 and H_2O. These experiments involve (1) linear potential scans of ammonium chloride, urea and glucose plus urea in phosphate buffer solutions and (2) anodic oxidation of glucose-urea in bicarbonate buffer in extra corporeal electrochemical cells.

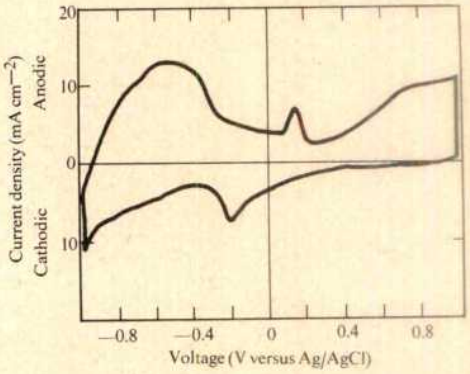

Fig. 1 Potential/current scan of 2.0 M urea in phosphate buffer (pH 7.4) on a Pt electrode.

An 'Electrochemistry System Model 170' (Princeton Applied Research Corp.) was used for the linear potential scanning studies. The system is similar to that used previously[6]. The working electrode was a smooth platinum disk, 1 cm^2. An Ag/AgCl reference electrode was used. The counter-electrode was a 4 cm^2 platinum black (40 mg Pt cm^{-2}). The electrolyte was Krebs-Ringer phosphate buffer at pH 7.4. Triangular potential sweeps were conducted over a range of -1.00 V to $+1.00$ V versus Ag/AgCl, that is, -0.32 V to $+1.68$ V versus RHE (Reversible Hydrogen Electrode potential at the pH of the solution), at a scan rate of 0.20 V s^{-1}. Potential/current curves were recorded on either an oscilloscope or an x-y recorder. The potential sequence used to achieve a well-defined Pt surface followed from that of Giner and Malachesky[7].

The general character of the scan closely resembles that of similar plots obtained in phosphate buffer by other workers[7]. Fig. 1 shows the cyclic scan recorded for 2.0 M urea in phosphate buffer. A time-variant oxidation peak appears at around 0.12 V versus Ag/AgCl, around 0.80 V versus RHE, in the anodic scans of the urea solution. The same peak appears in the glucose plus urea solution (0.80 M glucose and 2.0 M urea). It is not seen in the scans of both solutions of buffer alone and of NH_4Cl. The chemisorbed species at 0.80 V versus RHE has been tentatively identified as "reduced CO_2" for the glucose scan[7] and for scans of other carbonaceous compounds by Giner[8,9]. We

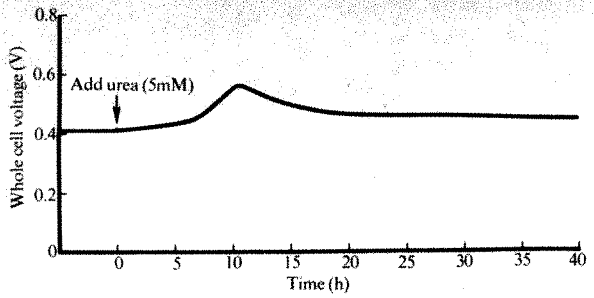

Fig. 2 Effect of added urea on an electrochemical cell operating with 5 mM glucose at the Pt anode, air at the Pt cathode and under 5 Ω load. Initial current density; 82 μA/cm^{-2}.

present here the first evidence that a similar adsorbed "reduced CO_2" species might be produced in the anodic oxidation of urea.

The presence of this chemisorbed species clearly indicates that urea can be directly oxidized at a Pt anode, possibly yielding CO_2, NH_4^+, N_2 and H_2O. Although it would be desirable that NH_4^+ is not a product it also can be oxidized to N_2 and H_2O at a Pt anode under physiological conditions[10]. Therefore, we conclude that the final products of anodic oxidation of urea are likely to be CO_2, N_2 and H_2O.

Experiments on de-ureation by anodic oxidation were carried out in extracorporeal electrochemical cells. A typical cell was made of a sandwich of electrodes and permselective membranes and assembled in a flow-through system[11,12]. The sandwich consisted of a hydrophilic Pt-black anode, an anion exchange membrane and a hydrophobic Pt-black cathode. The anode was covered with a cellulose membrane and was exposed to a flowing glucose-urea solution or plasma-dialysate (P_{O_2} 85 mm Hg, P_{CO_2}, 36 mm Hg and at pH 7.4). The cathode was in direct contact with flowing air. Current flow was produced either by shunting the cell with a resistor or by the application of an external d.c. power source. Fig. 2 shows the effect of added urea (5 mM) on an electrochemical cell operating with 5 mM glucose in bicarbonate buffer at the Pt anode, flowing air at the Pt cathode and under 5 Ω passive load. The cell voltage went up from 0.41 V to a maximum at 0.57 V within 12 h following addition of the urea to the glucose solution. Similar voltage enhancement by the effect of addition of plasma or its dialysate, both contain urea, to an operating implantable glucose fuel cell[12] consisting of a Pt anode and a Ag cathode has also been observed and will be reported elsewhere[5].

These investigations have provided evidence that urea could be anodically oxidized to end products such as CO_2, N_2 and H_2O. The development of an extracorporeal electrochemical de-ureator which utilizes Pt-black or other catalysts, electricity and air is feasible. This approach eliminates the step of action of urease on urea and the removal of NH_4^+ formed by urease action, by an expensive adsorbent such as zirconium phosphate[1-3]. The entire renal dialysis system could be made portable.

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Bacterial Identification by Microcalorimetry

Forrest[1] and other workers have shown that interesting data regarding bacterial metabolism can be obtained by microcalorimetry of growing cultures. In our investigations into the use of microcalorimetry as a means of differentiating one microbial species from another, we have obtained characteristic profiles for different members of the family Enterobacteriaceae by observing the heat produced during their growth in liquid media. The microcalorimeter (Instrumentation Laboratory, Inc.) used is of an experimental design operating at 37° C and having a response time of approximately 10 min. The long term baseline stability is 2% full scale or 0.8 μcal s^{-1} ml.$^{-1}$ over a 14 h measuring period. The profiles are recorded on a conventional 10 inch strip chart recorder with a paper feed of 1 inch h^{-1}. The inocula for the temperature equilibrated test vessel consisted of approximately 500 cells obtained by dilution of a logarithmically growing broth culture.

As a broad selection of different organisms was to be studied, a complex culture medium was considered preferable. After tests of several commonly used enrichment media, brain-heart infusion (BHI) was selected. To provide greater cultural uniformity, Baltimore Biological Laboratory lot 01602 BHI was used for all experiments.

Using a sample volume of 4 ml. and observing the growth of the organisms in BHI over periods of 8 to 14 h, we have obtained curves of heat production against time. The complexity of the curves (Fig. 1) should be noted. Forrest[1] showed that heat production ceases abruptly following the exhaustion of available glucose by *Streptococcus faecalis*. Our results show the same phenomenon for that organism in BHI. Sudden changes in heat production occur at many successive points during the growth of some organisms in BHI, as illustrated in Fig. 1. Some peaks are seen which last only a few minutes. Curves for a given organism are virtually superimposable in repetitive experiments. Using these curves we can discriminate between all Enterobacteriaceae yet tested which has included 17 species from 10 genera. *Enterobacter aerogenes* and *Klebsiella*, which are very similar with respect to their behaviour in biochemical tests, are clearly different in respect of their heat production. Some strains of *E. cloacae* can be separated from each other, although each possesses characteristics which permit species identification.

We are presently engaged in a detailed study of the use of microcalorimetry in identification of the organisms encountered in the clinical microbiology laboratory. The evidence indicates

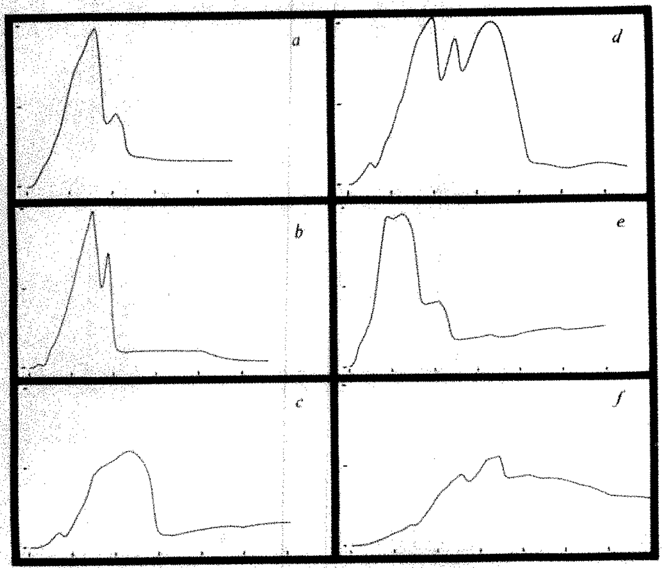

Fig. 1 Six named heat profiles are shown. For each, the abscissa represents time, with 2-h intervals indicated by scale marks, and the ordinate represents heat production, with scale marks at 0, 20, and 40 μcal s^{-1} ml.$^{-1}$. *a*, *Enterobacter aerogenes*; *b*, *Klebsiella*; *c*, *Proteus vulgaris*; *d*, *Enterobacter cloacae*; *e*, *Escherichia coli*; *f*, *Proteus rettgeri*.

that this approach provides a means for rapid and specific characterization of members of the Enterobacteriaceae. Organisms which do not grow well in broth cultures because of special metabolic needs present problems to be solved. However, for the great bulk of the organisms which must be identified in the routine laboratory, microcalorimetry represents a powerful tool. For research purposes, microcalorimetry provides highly informative data regarding microbial metabolism.

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Nitrosopyrrolidine and Dimethylnitrosamine in Bacon

Dimethylnitrosamine (DMN) and, in general, many N-nitrosamines are extremely potent carcinogens[1,2], and trace amounts of DMN have been demonstrated in certain types of cured meat products and smoked fish[3–5]. Certain press reports[6] in the United States have indicated that significant amounts (up to 0.106 p.p.m.) of nitrosopyrrolidine (NPy) can be formed during the cooking of nitrite-treated cured bacon. Data seem to be very scanty, however, and details have not been published in the scientific literature. Here we provide conclusive evidence for the presence of both DMN and NPy in bacon.

The bacon was purchased from local stores and analysed as such or after frying in an electric pan. The samples were extracted, and the nitrosamines in the extract purified by a method reported earlier (N. P. Sen, presented at the International Agency for Research on Cancer Meeting on the "Analysis and Formation of Nitrosamines", Heidelberg, 1971). The amount of DMN in the final extract was semi-quantitatively estimated by gas-liquid chromatography (GLC) using a Coulson electrolytic conductivity detector operating in the pyrolytic mode[7,8]. This detector, under such conditions, is specific for ammonia, amines, and compounds such as nitrosamines that produce these products upon pyrolysis. As free amines and ammonia are removed in the clean-up procedures, very few compounds are present in the final extract that can interfere with the analysis. A level of 0.002 p.p.m. DMN in meat can be detected and the recovery of DMN added to bacon at 0.01–0.02 p.p.m. levels was about 70–80%.

NPy was detected by a specific thin-layer chromatographic technique developed in this laboratory. About 0.1–0.3 ml. of the final extract (1 ml.) was spotted on a silica-gel plate and analysed by the method described earlier[9] Acetic acid-ninhydrin reagent combination[9] was used for the final detection. NPy appeared as an orange fluorescent spot when the heated plate was examined inside a 'Chromatoview' chamber (Ultra-Violet Products Inc., San Gabriel, California). Both the short-wave and long-wave transilluminator ultraviolet lamps were used for detection. This technique is very sensitive as well as specific, 50 ng NPy producing a clearly visible spot.

The amount of NPy present in the extract was semi-quantitatively determined by visual comparison of the intensity and size of the spots with that of authentic standards. The detection limit is about 0.005–0.01 p.p.m. of NPy in bacon and other meat products, and the recovery of added NPy (at 0.01 p.p.m. levels) varied between 60–80%. In a few cases, the initial extraction step was omitted and NPy was isolated by direct vacuum distillation of the product in the presence of 3 M potassium hydroxide. This modification resulted in a much better clean-up, and it was possible to detect NPy at 0.002–0.005 p.p.m. levels.

Table 1 Levels* of Nitrosopyrrolidine and Dimethylnitrosamine in Bacon

Sample No.	Kind	NPy p.p.m.	DMN p.p.m.
1	Side bacon, fried	0.02	N.d.†
	Side bacon, uncooked	N.d.	N.d.
2	Side bacon, fried	0.025‡	0.004
	Side bacon, uncooked	N.d.	0.03‡
3	Side bacon, fried	0.01	0.002
4	Sliced bacon, fried	0.025	0.002
5	Sliced bacon, fried	0.01	0.002
6	Sliced bacon, fried	0.004	N.d.
7	Side bacon, fried	N.d.	0.002
8	Side bacon, fried	0.01	0.005

* Uncorrected for percentage recoveries.
† Not detectable.
‡ Results confirmed by GLC-mass spectrometry.

Altogether sixteen samples of bacon (both fried and unfried), five of baby foods containing bacon as one of the ingredients, and six of other meat products were analysed. Eight samples gave a positive test for either DMN or NPy (Table 1); all others were negative. It may be of interest that none of the raw bacon contained any detectable amount of NPy but one contained about 0.03 p.p.m. DMN. Because of its high volatility the level of DMN in this sample fell to about 0.004 p.p.m. on frying. From this limited data it would appear that NPy is formed during frying. As NPy is also fat-soluble the major portion would be expected in the cooked fat. In one sample (No. 5) about 70% of the total NPy was detected in the cooked fat.

The identity of NPy and DMN from sample No. 2 was confirmed by GLC-mass spectrometry using conditions published previously[4,8]. The fragmentation patterns of the isolated NPy and that of the authentic standard are very similar (Fig. 1), and both show strong peaks at m/e 100 (M^+) and 30 (NO^+). The isolated DMN produced strong peaks at m/e 74 (M^+) and 30 (NO^+) when analysed by GLC-mass spectrometry using a 'Carbowax' 20 M column[4], but the mass spectrum showed the presence of some other interfering compounds. Mass spectrometric confirmation was therefore carried out using a second GLC column ('Reoplex' 400)[4]. In view of the positive results with the GLC-mass spectrometric analysis on two columns, and a single peak on GLC analysis with the specific 'Coulson' detector we concluded that the compound was most likely DMN.

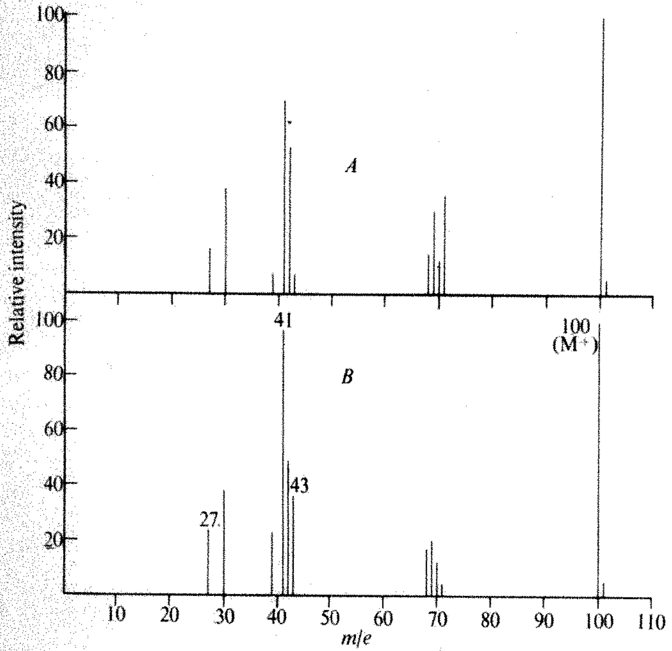

Fig. 1 Mass spectrum of NPy. *A*, NPy isolated from sample No. 2; *B*, NPy standard. The background signals (scanned just before the emergency of NPy peak) were subtracted in each case. A 'Hitachi Perkin-Elmer', RMS-4 mass spectrometer coupled with a 'Perkin-Elmer', Model 990, gas chromatograph was used. A 6 foot, 1/8 inch stainless steel column packed with 10% 'Carbowax' 20 M on 60–80 mesh 'Chromosorb' W (HMDS treated) was used for GLC analysis.

Although these values of NPy in bacon are much lower than that (0.030–0.106 p.p.m.)[6] reported by the US FDA laboratories, both these studies establish that trace amounts of NPy can be present in fried bacon. It is, however, not clear how NPy is formed during cooking. It can be produced in two ways: (*a*) formation of nitrosoproline from proline and nitrite and subsequent decarboxylation to NPy[10] or (*b*) by direct interaction of pyrrolidine, which could arise from proline or putrescine[11], and nitrite. Further research is needed to establish which of these, or any other reactions, is responsible for the formation of NPy in cooked bacon.

Both DMN and NPy are strong hepatocarcinogens in laboratory animals, although the latter is much less potent[12]. In the absence of reliable data on dose-response relationships at low levels it is difficult to assess the hazard to human health arising from the ingestion of trace amounts of nitrosamines in the diet. In view of the extreme carcinogenicity of these compounds in a wide range of species, however, it will be highly desirable to carry out further research which could lead to the control and eventual reduction of the levels of nitrosamines in meat products.

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Natural Inhibitor of the Gypsy Moth Sex Attractant

INHIBITION or masking of sex pheromone response by natural products occurring in the pheromone producing gland has been described in the gypsy moth[1], *Porthetria dispar* (L.), other Lepidoptera[2,3] and insects in additional orders[4,5] but none of the inhibitors has been identified. We report here that an olefin, 2-methyl-*cis*-7-octadecene, present[6] in the female sex pheromone gland of the gypsy moth, inhibits male attraction to the female sex attractant pheromone, which was identified as *cis*-7,8-epoxy-2-methyloctadecane[6].

Table 1 Mean Catch of Wild Males in Unbaited Traps and in Traps Baited with Attractant and/or Olefin Inhibitor

Treatments	Mean male catch/trap *
10 μg attractant	82.5 a
10 μg attractant + 1 μg inhibitor †	63.5 b
10 μg attractant + 10 μg inhibitor	46.0 c
10 μg attractant + 100 μg inhibitor	5.7 d
10 μg attractant + 1,000 μg inhibitor	8.7 d
Unbaited	0.3 e

* Means followed by the same letter are not significantly different at the 5% level. Treatments replicated four times.

† Olefin inhibitor alone at 1 μg to 1,000 μg attracted < 3.0 males/trap.

In field studies conducted in Connecticut, simultaneous evaporation of the attractant and its inhibitor from separate rubber septa wicks (Table 1) in sticky 'Sectar' traps ('Model XC-26', 3M Co.) shows that even low release rates of the olefin suppress male attraction, whereas somewhat higher release rates of olefin effectively inhibit attraction. More importantly, at these same release rates the olefin also eliminates the attractiveness of live calling females (Table 2, Experiment 1).

The *raison d'être* for the inhibitory action of the olefin may be due to competition for the same olfactory receptor sites as the attractant on the male antennae. This was suggested as a mechanism for inhibitory effects of certain compounds structurally similar to sex attractant pheromones[7,8]. Although it seems that the olefin is a precursor to the pheromone[6] we also considered possibilities for its natural release to control behavioural activity of the males. Females mate only once and mated females usually do not lure males[9]; by releasing the olefin an inseminated female could escape copulatory attempts by males and would thus deposit her eggs unmolested. Our field tests suggest, however, that females release little or no olefin after mating (Table 2, Experiment 2), for although freshly mated (and hence non-calling) females are not attractive, an attractant wick added to traps baited with freshly mated females (Table 2, Experiment 3) is attractive and apparently is unaffected by the mated female.

Table 2 Mean Catch of Wild Males in Sticky Traps Baited with Caged Mated or Unmated Females Compared with Catch in Presence or Absence of Attractant or Olefin Inhibitor

Treatments	Mean male catch/trap
Experiment 1	
Virgin female	44.0 a*
Virgin female + 1,000 μg inhibitor	1.3 b
Experiment 2	
Virgin female	27.7 a*
Freshly mated female	0.5 b
Experiment 3	
Freshly mated female + 10 μg attractant	13.2 a*
10 μg attractant	11.4 a

* Means followed by the same letter are not significantly different at the 1% level. Treatments replicated four times.

The behavioural effects of the olefin indicate that it might be more effective than the attractant in disrupting the gypsy moth communication system in field trials[10] in which areas are flooded with numerous sources of chemical for suppression of this important forest defoliator. The olefin would be particularly effective if it causes mating inhibition at the central nervous system level.

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Growth and Metabolism of *Ostrea edulis* Larvae

ONLY a fraction of the plant food captured by zooplankton is converted into growth; the rest is lost through incomplete assimilation, excretion and metabolism. The net growth efficiencies, K_2 (percentage of assimilated food converted into growth) for haloplanktonic animals such as *Calanus* and related copepod species are generally lower than the percentage of assimilated food lost in metabolism ($100-K_2$). In terms of calories, values of K_2 quoted in a recent review by Corner and Davies[1] range from 23–58 for *C. hyperboreus*, from 6–55 for *C. helgolandicus*, and from 14–29 for *Acartia clausi*. There are few comparable estimates of growth efficiencies for meroplankton species, such as molluscan larvae, but the data that does exist suggests that the values of K_2 are considerably higher than those for copepods. Jørgensen calculated a value for K_2 of 73% for *Mytilus* larvae and values of 62% and 63% for two gastropod veligers[2], and from short-term feeding experiments with *Ostrea edulis* Walne estimated that 68–80% of the total food assimilated by the larvae is utilized for growth[3]. During larval development the daily level of assimilated food declined from 56% to 29% of the body weight.

One of us (DLH) has recently published data on the changes in biochemical composition of *O. edulis* larvae during development and on the losses of the body components during short-term starvation experiments[4]. We have calculated an energy budget for *O. edulis* larvae from this data in terms of growth and metabolism.

Three batches of larvae, released between February and April, 1971, were reared at the MAFF Fisheries Experiment Station, Conway. The larvae were kept at 20–22° C in aerated seawater, and fed a mixed algal diet of *Isochrysis galbana* and *Tetraselmis suecica*. On release (day 0) and subsequently on days 4, 8 and 12, samples of approximately 10–15,000 larvae were collected for biochemical analysis at the NERC Unit of Marine Invertebrate Biology, Menai Bridge. The larvae were counted and analysed for protein, lipid and carbohydrate content as described previously[5]. Further samples of larvae were taken from the main culture vessels, on the days indicated, and placed without food in aerated seawater for 48 h before biochemical analysis.

Table 1 Protein, Lipid and Carbohydrate Content (mg per 10^6 larvae) of *Ostrea edulis* Larvae during Development

Days after release	Length (μm)	Protein	Lipid	Carbohydrate	Total calories
0	179.3	118.3	29.8	14.4	1,009
4	221.9	309.1	121.7	42.5	3,070
8	266.2	610.4	249.1	67.3	6,079
12	296.8	1,083.6	543.7	130.2	11,794

Tables 1 and 2 show the biochemical composition of *O. edulis* during development (mean values for the three experiments) and the mean losses of protein, lipid and carbohydrate on starvation. The results are expressed in terms of 10^6 larvae. *Ostrea edulis* larvae can survive for several days without food. During this time the necessary energy is derived from reserves in the body tissues and the total energy loss, during starvation, can be taken as an estimate of the metabolic energy demand. Conventionally metabolic rates are calculated from measurements of oxygen consumption during respiration. There is reasonably good agreement between the loss of body reserves and experimentally determined rates of oxygen consumption for newly released *O. edulis* larvae[6]. This need not necessarily be true however, as for example, when there is a partial anaerobic metabolism. As a first approximation we have used the data from the starvation experiments to calculate metabolic rates for *O. edulis* larvae.

Table 2 *Ostrea edulis.* Loss of Protein, Lipid and Carbohydrate (mg per 10^6 Larvae) During Starvation for Two Days

Days after release	Protein	Lipid	Carbohydrate	Total calories
0	10.2	8.1	1.4	140
4	20.2	45.0	10.4	582
8	74.9	74.5	4.2	1,144

On release (days 0–2) the daily loss of body reserves is equivalent to an oxygen consumption rate of 0.6 μl. 10^{-3} 0_2 per larva h^{-1}. This value is close to the value given by Millar and Scott[6] for newly released larvae kept without food at densities in excess of 100 larvae ml^{-1}. The daily loss of reserves for days 4–6 and 8–10 are equivalent to oxygen consumption rates of 2.5 and 5.0 μl. 10^{-3} 0_2 per larva h^{-1} respectively. The former value is approximately half the rate determined by Walne for larvae of the same size range feeding on *Isochrysis*[7]. Zeuthen concluded from measurements on individual *Mytilus edulis* larvae that the rate of oxygen uptake for "resting" metabolism was approximately half the rate for "swimming" metabolism[8]. In Table 3 we have equated our calculated values for the metabolic energy demand during starvation with resting metabolism and doubled these values to obtain the figures for swimming metabolism.

Table 3 Growth and Metabolism of *Ostrea edulis* Larvae

Days after release	Energy values: calories per 10^6 larvae day^{-1} Growth	Metabolism Resting	Metabolism Swimming	Net growth efficiency(K_2)
0–2	515	70	140	78.6
4–6	752	291	582	56.4
6–10	1,429	572	1,144	55.5

The net growth efficiencies K_2 for swimming larvae fell from 78.6% on release to 55.5% on day 10. The daily food requirements (assimilated ration) to support growth and metabolism represented 64.9% and 42.3% of the body weight on day 0 and day 10 respectively.

The values of K_2 are probably conservative estimates because of doubling of the energy loss during starvation to give the level of swimming metabolism. Oyster larvae, for example, when released from the adult can survive for several days without food and can be swimming actively during this time[6]. Based on the data for resting metabolism the corresponding values for K_2 would be 88.0% on day 0 and 71.4% on day 10. Our calculations, therefore, confirm the view that molluscan larvae have high net growth efficiencies[2,3], such that 50–80% of the assimilated food is utilized for growth. Whether or not such high values are limited to young, rapidly growing stages needs further study. Corner and Davies[1], quoting data obtained by Petipa from the Black Sea, suggested that K_2 values for young copepodite stages are higher than those for older animals, although in terms of body nitrogen it is the older stages that show the most rapid growth[9].

Finally, the total energy demand (growth plus metabolism) can be compared with published data on the rate of consumption of *Isochrysis* by oyster larvae at different stages of development[3]. Walne gives values of 395–600 cells per larva h^{-1} for larvae of mean length 178 μm and 916–1517 cells per larva h^{-1} for larvae of mean length 219 μm. These values can be converted into calories (10^6 cells$=$0.016 mg dry matter$=$0.09 cals) and used to give an estimate of assimilation efficiencies on day 0 and day 4 respectively. The calculated values for assimilation efficiency range from 50.8–77.1% on release to 40.9–67.7% on day 4. Although it is recognized that these values are necessarily approximate they are considerably higher than the values of 15–45% calculated by Walne[3] from feeding experiments with ^{32}P-labelled algae and are comparable to the values reported for *Calanus*[1].

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Antibody to *Babesia* in Scottish Red Deer *(Cervus elaphus)*

Babesia spp. have a world wide distribution in domestic animals[1]; and have also been described in wild animals[2,3]. The occurrence of this protozoon, however, is poorly known since the organism is rarely detectable in blood films except for a short period soon after initial infection. After this time, if the host survives, the infection becomes latent. Infections may be diagnosed by serological methods. The indirect fluorescent antibody (IFA) test has the practical advantage that it is simple to perform and requires only a small volume of serum; it can also be carried out with blood collected on filter paper.

Babesia spp. of domestic animals are thought to be host specific. Callow[4], however, has shown that when ticks infected with *B. bigemina* were allowed to feed on sheep, viable parasites appeared in the blood. When blood was transferred from sheep into susceptible calves, an obvious infection with *B. bigemina* developed.

It has also been shown that when *B. divergens* and *B. motasi* were introduced by blood inoculation into splenectomized red deer, *B. divergens* persisted for at least 230 days and *B. motasi* for 100 days, in the blood stream[5,6]. In Scotland, many tick infected pastures are shared by cattle, sheep and red deer. In some areas *B. divergens* has been reported in the cattle, and we thought it would be of interest to look for babesial antibody in red deer.

Normal serum was obtained from deer which had been born and reared at the Rowett Research Institute, Aberdeen. A globulin fraction was prepared by precipitation in 50%

ammonium sulphate. An antideer globulin was obtained by intradermal injection into rabbits of the globulin fraction in Freund's complete adjuvant. The globulin fraction of this serum was separated by ammonium sulphate precipitation and conjugated with fluorescein isothiocyanate (isomer I, Sigma). Excess dye was removed by filtration on a 'Sephadex G-25' column, and non-specific fluorescence was removed by absorption with rabbit liver acetone powder (Sigma).

Sera or blood on filter paper from 25 deer shot in Ross-shire and Inverness-shire and blood samples from Arran were examined. The IFA test was performed as described by Brocklesby *et al.*[7] with *B. divergens* as the antigen.

The sera of 7 out of the 25 mainland deer had babesial antibody; the titres of the sera ranged from 1/40 to 1/320. One of the 2 blood samples from the Arran deer fluoresced brightly when the antigen was treated with eluate from the filter paper. Fluorescence was absent when the antigen was treated with normal deer serum at dilutions greater than 1/10. The titres of the deer sera were similar to those found in a survey for babesiasis in cattle on the island of Arran[8].

The results indicate that red deer in Scotland are parasitized by a *Babesia* sp. We believe that this is the first record of this parasite in red deer in Britain[9], although *Babesia* has been found in deer in other parts of the world[10,11].

We thank members of the South Ross Deer Unit of Edinburgh University and Mr J. Logan, Corrie, Arran, for supplying samples of blood from red deer; Mr. G. A. M. Sharman of the Rowett Research Institute, Aberdeen, for supplying normal deer serum and Dr L. P. Joyner, Central Veterinary Laboratory, Weybridge, for supply calf blood infected with *B. divergens.* We also thank Mrs J. Riddaway, for advice on methods for the separation and conjugation of globulins. B. M. A. L. is in receipt of a scholarship from the Calouste Gulbenkian Foundation, University of Baghdad.

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Chimpanzee Tool Use in Dental Grooming

TOOL use by animals is characteristically restricted to agonistic, exploratory, or self-maintenance contexts, and we have only one record of its use in social grooming[1]. Belle, a female chimpanzee (*Pan troglodytes*) at the Delta Regional Primate Research Center, used sticks as aids in grooming the teeth of other individuals, and on one occasion she fashioned a stick tool by stripping a twig of its leaves. In 135 h of observation over 6 weeks, we recorded forty-five bouts of dental grooming: four of tool use (all social), twenty-three of social grooming, seven of attempted social grooming, and eleven of self grooming. Dental grooming occurred on 16 of the 27 observation days.

The main cause was probably Bandit's (the youngest male) shedding of deciduous molars. His teeth had two fresh vacancies and one loose movable tooth barely in place. In some cases Belle definitely concentrated her efforts on these sites.

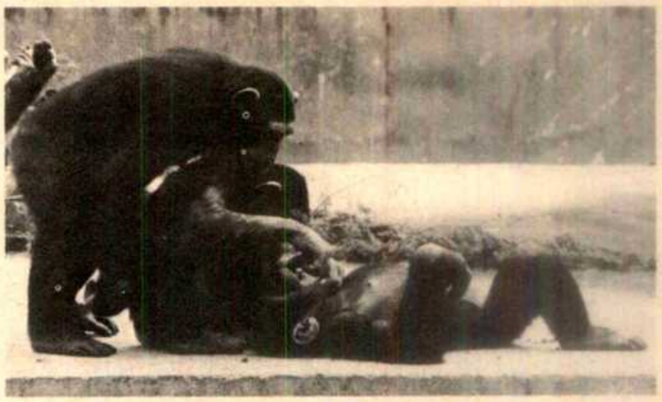

Fig. 1 Belle (sitting) dental grooms the teeth of Bandit (lying supine) with a small pine twig tool. Shadow (standing bipedally) looks on.

Seven adolescent chimpanzees (aged 7–11 yr) lived as a group for 3.5 years in a one acre outdoor enclosure carpeted with natural herbaceous vegetation and containing over seventy upright or fallen poles and tree trunks. Fresh branches and saplings were introduced weekly. We observed the group's activities from an overhead observation deck using binoculars and a camera with a telephoto lens.

In all four instances of tool use in dental grooming, Belle was the "dentist" and Bandit the "patient" (Fig. 1). Her usual procedure was to begin normal social grooming directed to the hair of his limbs, torso, or head. She then concentrated on his face and, finally, opened his mouth. If he cooperated by gaping his jaws, she began dental grooming with the fingers, accompanying this with "teeth clapping", a sound produced during high intensity grooming by rapidly banging the teeth together. Sticks used as supplementary aids were picked up from the surrounding substrate, apparently on the spur of the moment. The single case of tool modification occurred on the day after red cedar (*Juniperus virginiana*) branches had been introduced, and the area around the grooming pair was littered with fragments (see background of Fig. 1). Belle picked up a twig approximately 0.5 cm in diameter and stripped off the leaves, leaving a pencil-like object about 15 cm long. Between sessions of using it as a pick, she left it hanging loosely out of the corner of Bandit's mouth, or held it between her own lips like a cigarette, or rested it on his chest if he were lying supine. Several tools have been recovered (Fig. 2), and all have scraping or probing edges. The tool-using grooming bouts were protracted: 730, 530, 300, 185 s in length. Ordinary social grooming bouts averaged 114 s in duration ($N=202$, range: 5–1,779). Following dental grooming, Belle returned to normal grooming of other body parts.

Belle was also responsible for twenty-two of the twenty-three dental social grooming bouts without tool use. Bandit received eighteen of these, and Shadow (another male) received four. Her general procedure resembled that already described. She commonly used her thumbs as scrapers and her forefingers to pick particles loose. These were rapidly flicked out of the mouth, or, more uncommonly, the two forefingers were used together as forceps to remove the particle. She apparently concentrated picking on molars and scraping on incisors. She seemed to be equally dextrous with either hand, and she sometimes supplemented her hands by using her lips. Her usual practice involved using one hand to steady the patient's head while working with the other. When grooming the lower teeth, she hooked the opposite-hand thumb under the upper jaw and spread the fingers over the forehead. When working on the upper teeth, she held the lower jaw maximally gaped with the non-working hand. Belle adopted a variety of postures while working: sitting, bipedal standing, crouching, reclining. The patient usually lay supine, but Belle manoeuvered him through other postures. Dental social grooming bouts not

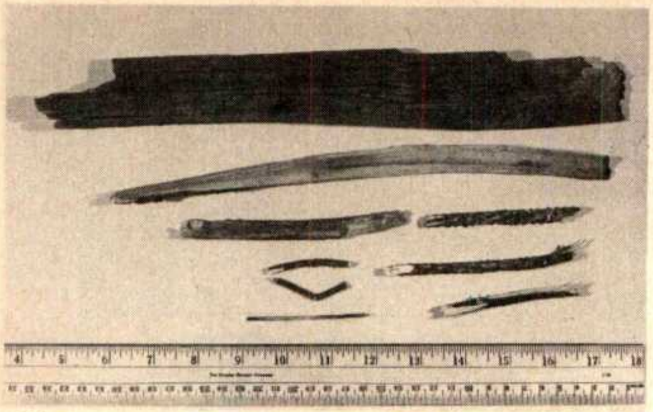

Fig. 2 Range of wooden tools used by Belle in social dental grooming.

involving tools averaged 56 s in length ($N=18$, range: 10–283). These were significantly shorter than dental grooming bouts involving tools (Mann-Whitney U test, $U=1$, $P>0.002$, two-tailed).

Belle also exhibited all the unsuccessful attempts at dental grooming and directed these to four different individuals. They followed a consistent sequence: Belle groomed another chimpanzee normally, then switched her manipulations to the groomed animal's mouth. The latter compressed its lips and turned away its head (and in one extreme case, covered the face with the forearms). This prevented further dental grooming and Belle returned to normal grooming. In one instance, however, she responded to Bandit's refusal to be dentally groomed by flipping his lower lip down. This everted it over his chin, and she continued dental grooming in spite of his clenched teeth. Her unsuccessful attempts were of short duration, the longest lasting 13 s.

We saw six of the seven chimpanzees groom their own teeth, and no single individual exhibited a disproportionate share of the group's total. The thumb was usually used to groom the upper teeth and the forefinger used to groom the lower teeth. We saw no self grooming tool use, but wild chimpanzees commonly use tools in grooming their external body surfaces. They remove sticky substances by wiping with leaves and branches, and water by rubbing against tree trunks. Only great apes have been seen to use tools in self grooming of body orifices: van Lawick-Goodall presented one case each of chimpanzee self grooming of the teeth and nose with twigs[2]. Captive chimpanzees may use mirrors as visual aids to pick at their own teeth and nostrils[3].

Apart from its hygienic function, primate social grooming is the most common socially affinitive behaviour, involving prolonged intimate physical contact, and it presumably reinforces social bonds and thereby has ramifications in social organization and structure[4,5]. Miles inferred the presence of altruistic intentions in grooming to relieve the discomfort of afflicted individuals[6]. Yet only once before has the use of tools been recorded in this important primate activity. Van Lawick-Goodall saw a wild female chimpanzee use leaves to wipe sticky banana from the head of her infant sibling[2].

Recent observations have re-emphasized the chimpanzee's paramount position as a maker and user of tools amongst the non-human primates[7–11]. Yet the dental grooming reported here is the first systematic use of tools in friendly social interaction to be recorded. Of course, many primates are capable of complicated tool use under special laboratory or zoo conditions[12], often intentionally helped by human intervention, such as animal intelligence testing[13]. The spontaneous use of tools described here, however, was shown by animals living a self-regulating, natural life. Obvious antecedents of the activity such as copying human use of tooth picks could be ruled out, and no human reinforcement was given.

Why did this unique form of tool use appear in this group of chimpanzees? All the individuals were wild-born and did not arrive at Delta until at least 1–4 yr old. Previous comparisons of wild and captive born chimpanzees have shown the former's superiority in the use of tools[14]. For most of their stay at Delta the chimpanzees lived in a large outdoor enclosure containing innumerable movable objects up to the size of telephone poles, and many novel objects were introduced over the years. Because the overall group of chimpanzees or subgroups of it were housed in mutual access from infancy, they had intimate, well-socialized relationships. This was exemplified in the broad latitude allowed each other in grooming. In addition to grooming each other's hairy body surfaces, they groomed each other's eyes, nostrils, ears, genitals and anuses.

Belle performed 97% of the social dental grooming observed (the exception was performed by a male to another female). She also showed the most frequent ordinary social grooming and the longest mean bout length of any individual in the group, and was one of the two most frequent tool users in other contexts. The other frequent tool user, Bandit, was the principal recipient of Belle's dental efforts, receiving twenty-four bouts. Shadow accounted for five, and two other chimpanzees two each. The subgroup of Belle, Bandit, and Shadow lived in uninterrupted contact from their arrival at Delta in June 1966, giving them the longest shared experience of any of the animals. If any substitute kinship relations existed in this group, this tryad (pictured in Fig. 1) was likely to possess them. Belle also directed 54% of her non-dental grooming to Bandit. He was apparently a most groomable individual; he received more grooming than any of the others and had the highest overall partner preference rank in social grooming although he rarely groomed others.

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Menarchal Age in Norway: Halt in the Trend towards Earlier Maturation

STATISTICS on the age at menarche have shown that girls have been maturing progressively earlier in all parts of Europe, North America and Japan during the past fifty years[1,2]. The rate of advance of menarche, about 4 to 5 months per decade, has been constant in all countries during this period. There is some evidence that this advance of the onset of puberty can be traced back to the middle of the last century in some countries, among them Norway[1]. There have been no published reports of a cessation of this trend, and Tanner[2] believes that the trend "may be extrapolated onwards for at least another decade or two".

Two different methods have been applied to obtain estimates of the age at menarche[3]. (1) Girls of the relevant ages have been asked whether or not they have experienced their first period (the *status quo* method). (2) Older girls or women have been asked about their age at their first period (the "recall" method). All information about the age at menarche in the nineteenth century was obtained by the recall method, and probably with very biased samples of the population. The *status quo* method was introduced by Schiøtz[4] in a study of schoolchildren in Oslo (Kristiania) in 1918, and has generally been accepted as the better of the two methods. Unfortunately, his first investigation involved only 177 girls aged 12 to 17 yr. His statistical calculations gave a mean menarchal age of 15.01 yr. Recalculations from his published tables by the numerical methods described here give a mean age of 14.57 yr and a standard deviation (s.d.) of 1.18 yr. Two large scale investigations, one by Schiøtz[5] in 1928 and the other by Letting[6] in 1952, were carried out using the *status quo* method on schoolchildren in Oslo. Each study involved about 10,000 girls 10 to 17 yr old. The published mean ages at menarche were 14.28 and 13.44 yr. Our recalculations give 14.18 yr (s.d. = 1.15 yr) and 13.27 yr (s.d. = 1.11 yr). In the period 1928 to 1952 the average advance of the menarchal age was 4.5 months per decade, a rate that agrees with results obtained in other countries[1,2]. Extrapolation of this trend to 1970 would predict a menarchal age of 12.6 yr.

Table 1 Percentage of Menstruating Girls at Each 3 Months of Age

Age group centres (yr)	Number of menstruating girls	Total number of girls	Percentage of menstruating girls
11.00	2	292	0.68
11.25	4	251	1.59
11.50	10	269	3.71
11.75	12	259	4.63
12.00	32	293	10.92
12.25	49	262	18.70
12.50	59	266	22.18
12.75	91	283	32.15
13.00	115	282	40.78
13.25	151	296	51.01
13.50	188	289	65.05
13.75	192	271	70.84
14.00	212	286	74.12
14.25	218	263	82.88
14.50	243	276	88.04
14.75	305	334	91.31
15.00	284	315	90.15
15.25	282	298	94.63
15.50	266	274	97.08
15.75	293	299	97.99
16.00	298	305	97.70
16.25	276	282	97.87
16.50	270	274	98.54
16.75	296	301	98.33
17.00	334	335	99.70
		7,155	

Our investigation, carried out in March 1970, included physical measurements in addition to questions about menstruation. Only the results concerning the age at menarche obtained by the *status quo* method will be published here. All primary and high schools in Oslo were included in the investigation; schooling is compulsory in Norway up to and including the age of 16, and 50% of the children continue in school for at least two more years. The results obtained from 7,155 girls are given in Table 1. The percentage of menstruating girls at each 3 months of age are plotted as a function of the centre of the age group in Fig. 1*C*. The mean menarchal age and its s.d. were estimated from this empirical cumulative menarchal age distribution by fitting a theoretical curve to it with a standard non-linear least-squares procedure. The theoretical functions were either a cumulative normal distribution calculated by a computer subroutine or a logistic function. Both functions gave identical results. The mean age at menarche in Oslo in 1970 was estimated to be 13.24 yr (s.d. = 1.04 yr). The corresponding logistic curve is plotted in Fig. 1*C*. The empirical data from Schiøtz and Letting's investigations are plotted similarly in Fig. 1*A* and *B* with the corresponding best fitted logistic functions.

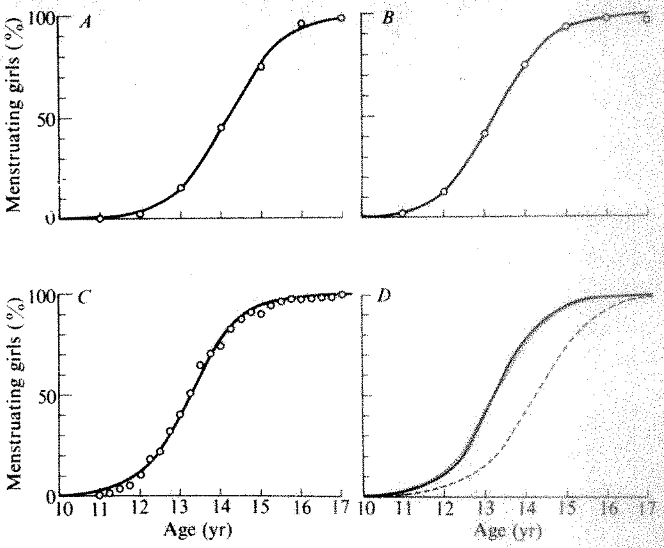

Fig. 1 Cumulative menarche-age distributions. *A*, 1928 empirical data from Schiøtz[5]. Line plotted from best fitted logistic function; $Y = 100.0/(1.0 + \exp(1.6675 * (\text{Par}(1) - X)/\text{Par}(2)))$ where Y: percentage of menstruating girls at the age X (yr) Par (1): mean menarchal age (MMA) (yr); Par (2): standard deviation (s.d.) (yr), MMA = 14.18 yr and s.d. = 1.15 yr. *B*, 1952 empirical data from Letting[6]. Line as in *A* with MMA = 13.27 yr and s.d. = 1.11 yr. *C*, 1970 empirical data from the present investigation. Line as in *A* with MMA = 13.24 yr and s.d. = 1.04 yr; *D*, The three best fitted theoretical distributions plotted in one figure. - - -, The 1928 curve; . . . , the 1952 curve; ——, the 1970 curve.

Although the mean menarchal age decreased from 1928 to 1952, it did not change at all from 1952 to 1970 (Fig. 1*D*). This result seems to be the first indication in any country of a halt in the trend towards earlier physical maturation. Both the methods used and the populations studied in the three investigations are probably as comparable as they can be in view of the fact that more than forty years elapsed between two of the studies. All investigations were carried out within the Oslo city school health system, originally organized by Schiøtz, and the changes in the city have probably been, in most respects, less than in many cities of comparable size.

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Mental Disorder and Season of Birth

MOST investigations of the relationship between season of birth and mental illness have found that a disproportionate number of patients with schizophrenia or manic-depression were born in the early months of the year[1,2]. Most of these studies can reasonably be criticized on the grounds that the samples of patients were (*a*) not representative of all patients, and (*b*) not comparable with the general population used as the basis of expectation, because seasonal distribution of births in a general population may vary significantly not only from year to year but between adjacent geographical areas in the same year[3]. Dalen's study[4] largely avoided these criticisms because his schizophrenic patients were representative of the whole of Sweden; he made a decade-by-decade comparison (P. Dalen, personal communication) of years of birth with the general population. He found a very significant excess of the patients had been born in the months January to March.

Here we report further evidence in support of this, using material we believe to be free from these criticisms. Since 1970, the month as well as year of birth of all persons admitted to psychiatric beds in England and Wales have been recorded, and we used data from all patients first admitted in the years 1970 and 1971 who had been born in England and Wales from 1921. These cases can have no sampling bias and their seasonal distribution of births may properly be compared with the general population of the same geographical area from the year 1921. It was not possible to compare seasonal distributions of month of birth between the two populations before 1939 as it is only from this date that the monthly number of live-births in England and Wales has been published. It was possible, however, to compare seasonal birth distributions in terms of the first, second, third and fourth quarters of the year as these numbers are available for England and Wales from 1921, and the psychiatric admissions in 1970 and 1971 can be regrouped into quarters of the year from the monthly distributions made available to us. The comparisons made by us are therefore undisturbed by any heterogeneities, for example, in variation between urban and rural geographical areas or in variation from year to year, because all these sources of variation are exactly balanced between the two series. The reservations one would have to make to this comprehensive statement are unimportant. The general population cohort born in the year Y will have been reduced due to death and emigration by the year $(Y+x)$ when admissions to hospital occur. Immigration does not enter the picture as persons not born in England and Wales are excluded from the figures. Emigration will have affected the general population cohort by the time in the year $(Y+x)$ when psychiatric morbidity begins to operate, but there is no factual or plausible ground for supposing that emigrants differ in season of birth from the population from which they come. Deaths may, of course, influence the distribution of season of birth in the total population in the years after year Y if, for instance, infants born in one or another season have a higher or lower mortality than others. We consider it exceedingly improbable, however, that there has been any such effect operating on the population as a whole, indifferently of any potentiality to psychiatric morbidity; it can be seen from Table 1 that there is no shift in distribution of season of birth for psychiatric patients as a whole but only for two diagnostic sub-groups, the manic-depressives and the schizophrenics. Only in these two diagnostic groups is a statistically significant shift displayed.

Table 1 shows the observed and expected numbers of births in the first quarter-year for five diagnostic categories. The expected numbers are calculated as follows. If $N_{s\,(1921)}$ is the total number of schizophrenic patients born in 1921 and admitted to hospitals in the years 1970 and 1971, B_{1921} is the total number of live-births in England and Wales in that year, and F_{1921} is the number of that total born in the first quarter, then the number of schizophrenics, born in 1921, who could be expected to have been born in the first quarter is $N_{s\,(1921)} \times F_{1921}/B_{1921}$. All these yearly expectations are summed from year to year to give the total number of expected first-quarter-born schizophrenics for all years up to 1955, so as to provide the schizophrenia total (Table 1). The same procedure was used to calculate the expectations in the other four diagnostic groups. The total expected was then set against the total observed, and one degree of freedom used to estimate the significance of χ^2.

Table 1 Observed Numbers of Patients* (by Diagnosis), Born in the First Quarter of the Year Compared with Expectation from all Live Births in England and Wales†

Diagnosis	Total patients	Nos. in first quarter Observed	Expected	Ratio O/E	χ^2 (1 d.f.)‡
Schizophrenia	5,139	1,383	1,292.1	1.07	8.55
Manic-depressive psychosis	3,523	961	883.3	1.09	9.13
All other psychoses	2,852	708	713.9	0.99	0.06
Neurosis	12,061	3,056	3,024.2	1.01	0.45
Personality disorder	4,479	1,114	1,127.8	0.99	0.23

* All patients born in England and Wales 1921–55 and first admitted to a psychiatric unit 1970 or 1971.

† Sum of year-by-year comparison.

‡ First quarter and the remaining part of the year.

Table 1 shows that for schizophrenia and for manic-depressive psychosis there is a significant excess of births in January to March ($P<0.01$). The observed numbers in the other diagnostic groups differ only very slightly from expectation. The trend for each diagnosis is the same when the two years of admission are considered separately.

We think these results are important because they add substantially to the evidence for a real association between season of birth and functional psychosis. If real, this is the first association to be demonstrated between the incidence of schizophrenia and a clear-cut, objectively measurable, environmental factor. Moreover, the strength of the association is far from being negligibly small; births in the first quarter exceeded expectation by 7% for our schizophrenic patients, and by 9% for our manic-depressives (for the other diagnostic groups, the difference from expectation was about 1%). There are, of course, many non-causal explanations, the most obvious being a deviance in parental conception habits (in which case the birth pattern of the patients should also be shown by the patients' siblings). Social class differences in season of birth are not likely to be important here, for there is now good evidence that the fathers of patients with schizophrenia and manic-depression do not differ from the general population in their social class distribution[5–7].

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BOOK REVIEWS

Macromolecular Chemistry

Polymer Science: a Materials Science. Edited by A. D. Jenkins. Vol. 1. Pp. xxiii+1–932. Vol. 2. Pp. xxii+933–1822. (North Holland: Amsterdam and London, 1972.) Dfl. 380; $119.

It is now almost half a century since Hermann Staudinger propounded his theory of macromolecular chemistry, and faced opposition from the might of (mainly German) classical chemists. This was not so much based on chemical fact, albeit his results were attributed to the examination of impure products, as that he had the temerity to put forward his macromolecular theory as a new branch of organic chemistry. That Staudinger's claim was if anything an understatement is amply supported by the two volumes edited by A. D. Jenkins under the broad title of *Polymer Science.* From the ample references associated with the 1,800 pages of the text, it can readily be accepted that more than half of the present chemists throughout the world work in or are associated with polymer or, more broadly, materials science.

In the preface to the first volume the editor explains that he aims to provide a "vocabulary for those who come to the subject with little previous knowledge of polymers", a statement which after performing the daunting task of reviewing the two volumes must raise some elements of doubt. Basically the work deals with those "properties of polymers which call for physical examination and upon which the performance of polymers as useful materials depends". To attain this end he has adopted what is by traditional standards a novel approach to the subject, by devoting the first two chapters (191 pages) to the principles and methods of polymer production and their chemical structure, mentioning individual materials rather as incidental illustration of basic theory. In view of the spate of literature which has appeared dealing with specific polymer families or individual members, this is to be applauded, although the level of treatment now presented is likely to tax the understanding of those wishing to obtain the general "vocabulary and background" referred to by the editor.

The succeeding eleven chapters, which constitute the first volume (929 pages), deal with the physical properties of plastics from various aspects, ranging from the near esoteric consideration of theories of chain coiling, elasticity and viscoelasticity to plasticization which comes very near to the production area. The various physical characteristics, such as glass transition, melting point and structure; crystallinity, fracture; optical properties, and the mechanical properties both of plastics and of fibres and fibre assemblies, are separately treated. The sequence of treatment may appear illogical, but this is of small consequence since each chapter is self-contained and is virtually a monograph on the selected subject, complete with references to relevant literature. Reference is made to specific polymers mainly as illustrative of the selected property, which means that data on any material are somewhat fragmented.

The second volume begins with a relatively brief study of adhesion, considered from the viewpoint of adhesive bonding as being the force required to separate substrates that are bonded together by means of an adhesive. The theory is supported by reference to a number of commercial polymers where problems of adhesion are frequently encountered. The following chapter on "Friction and Wear" will be of interest both to the practical man and to the theorist, particularly in view of the increased importance of polymers for applications in tribology. The next chapter, on "Polymer Solutions and Fractionation", although highly theoretical, has practical significance, because polymer solutions have been largely used to evaluate problems of structure, and their solution (and in some cases fractionation) plays an important part in their commercial applications. The four chapters devoted respectively to polyelectrolyte electrical properties, and two devoted to dielectric properties, have essentially a bias towards theory, but contain useful data for the practical man in this important area of polymer application. A more detailed study of the far infrared spectra of polymers is next given, from the viewpoint that it has long been appreciated that these data not only give an indication of the utility of polymers as transmissive media, but also details of the conformation of chains and of the interatomic forces operative in and between them. The study of nuclear magnetic resonance (n.m.r.) given in the following chapter is shown to be applied not only to basic problems of polymer structure, but also to obtaining information concerning the motion of polymer molecules. This is an area which the author rather modestly concedes as being at present "mainly in the hands of specialists". The chapter on "Degradation" is broadly interpreted as covering any sort of chemical change. The possible progressive change in the physical properties (and hence performance) of plastics materials has for long been among the major causes of their rejection by some industrial users, so that the basis of the trouble and the possibility of avoiding it are of practical importance. Closely related to this subject, and separately considered under the general heading of "Radiation Effects", is a brief review of the physical and chemical changes brought about by the exposure of polymers to high energy radiation. No references to related literature are given in this instance, which might be interpreted that the subject is now less highly rated than was earlier anticipated.

"The Identification and Analysis of Plastic Materials", a very important chapter dealing with a subject which almost defies brief treatment, might be considered as more relevant to the technology than to the science of polymers. Some aspects of the subject have inevitably been treated in other chapters, but copious references compensate for lack of detail. The next two chapters, dealing respectively with polymers for use at low and high temperatures and with composites, have the common factor that they are contributed by recognized experts in the aircraft industry, which is possibly plastics' most exacting end-user. Even allowing for the space limitations there are some surprising omissions from the heat-resisting polymers; the organo-metallic compounds in particular appear to have been neglected. The chapter on composites is essentially technological, although there may be a difference of opinion as to where science ends and technology begins. There is certainly no doubt about the scientific nature of the final chapter on "Neutron Spectroscopy", which briefly outlines the theory of neutron inelastic scattering, or more basically of the binding forces in solids.

From this necessarily brief outline it is evident that the two volumes do full justice to the title. There is inevitably, as the editor admits, some overlapping of subject matter, but this is useful as giving viewpoints by different experts and in most cases based on different scientific disciplines. After careful consideration of the extensive text it is difficult to agree with the editor's claim that it will help anyone "encountering polymers for the first time to obtain a detailed understanding of the present level of appreciation of the nature of polymer behaviour in any selected field". Rather one must conclude that it is the book for the expert and those concerned with research and development in specific fields. The references in each chapter (classified alphabetically by author) give an excellent guide to the collected literature up to 1968/69. The indexes are adequate, but in view of the extent of the subject matter, a more detailed subject index would have facilitated quick reference. Inevitably the cost of these volumes is high, and must limit circulation even to libraries. Having regard to the specialist nature of each chapter it might have been more profitable alike to publisher and reader to split this enormous field, making each chapter (with perhaps a little judicious pruning) into a separate monograph. These volumes should at least find a place in every library concerned with polymer research.

V. E. YARSLEY

Nuclear Shell Guide

The Practitioner's Shell Model. By George F. Bertsch. Pp. viii+206. (North-Holland: Amsterdam and London, 1972.) Dfl. 36; $10.50.

FOR more than twenty years the nuclear shell model has been the model on which nuclear physicists have based most of their understanding of the structure of atomic nuclei, and few of us have been happy with alternative models until some understanding of their relation to the shell model has been obtained. There is an enormous variation in the degree of complexity of explanations of nuclear properties based on the shell model, which range from the prediction of spins and magnetic moments of nuclear energy levels from the quantum numbers of a single particle to the huge matrix diagonalization programmes for the configuration mixing of several particles. This book is an attempt to describe the middle ground between these two extremes where physical insight takes the place of elaborate calculation. The author is well qualified to write such a book, because he has done much with this approach.

The first two chapters give brief accounts of Hartree-Fock theory and the shell model, and of harmonic oscillator wave functions. The essentials of angular momentum theory and recoupling are presented in the third chapter. In the fourth chapter the nuclear interaction used in shell model calculations and its relation to the free nucleon-nucleon interaction are discussed. Chapter 5 is devoted to the effects of this interaction in nuclei in which only two particles (or a particle and a hole) are free to respond, while chapter 6 is concerned with configurations of several particles and the development of deformations of the nucleus. The next chapter deals with the effects of polarization of closed shells, which can alter both the effective interaction between particles, and their effective charges and moments. The final chapter discusses the information that can be obtained on shell structure from direct nuclear reactions by using the distorted wave Born approximation. At the end of each chapter there are problems with worked solutions.

The book is a valuable contribution to the subject, and the power and limitations of this approach should be understood by anyone who wants to work with detailed shell model calculations, or to teach students about the shell model. It is not in any sense a comprehensive guide to all aspects; many important areas are either completely omitted or barely mentioned. The classification of states by means of group theory has been very important, but there is no detailed discussion of it here. Pairing and the random phase approximation are omitted on the grounds that they are adequately treated elsewhere, but there is not even a proper explanation of the importance of short range forces for producing pairing; it might be thought from the remark made on page 98 that there is as much correlation of two particles in the state of maximum angular momentum as there is in the state of zero angular momentum. Within its limitations the book provides a clear and concise guide to important aspects of the nuclear shell model.

D. J. THOULESS

Neutron Activation

Neutron Activation Analysis. By D. De Soete, R. Gijbels and J. Hoste. Pp. xx+836. (Wiley: New York and London, July 1972.) £14.

THAT this large and comprehensive treatise on neutron activation analysis fills a real need is evident from the constant demand for the copies in my laboratory. The volume, the thirty-fourth in the Wiley–Interscience series of chemical analysis monographs, describes within its compass of almost 900 pages most aspects of neutron activation analysis and associated techniques.

The comprehensive nature of the work is best indicated by a brief survey of the contents. Two introductory chapters are followed by a detailed account of neutron-induced reactions and then, in chapter 4, a description of the various neutron sources—reactor, accelerator and isotopic—and of their operation. The next two chapters, dealing with the radioactivity growth and decay laws, radioactive disintegration and radiation detectors, are followed (chapter 7) by a consideration of the preparation of samples and standards. Chapters 8 and 9 describe respectively activation analysis with and without post irradiation radiochemical separation and the next two chapters discuss systematic errors and the statistical interpretation of results. Chapter 12, mainly a bibliography of the field, is followed by seven appendices containing tables of cross-sections for thermal, fission and 14 MeV neutron reactions, lists of radionuclides in order of gamma ray energy, gamma ray mass attenuation coefficients and chemical yield data.

It is not to be expected that a work of this sort will be completely free of errors or omissions, but those there are are not serious. A book which considers in detail, for example, diffusion of neutrons, beta ray theory, reactor physics and so on might also be expected to describe all major relevant chemical procedures. But for some of the most common of these—ion exchange, for example—the reader is directed to other works, although these are not specified. Nor does there appear to be any discussion of the important allied technique of capture gamma ray analysis.

The index is unsatisfactory and should be made much more comprehensive in any future edition. Also the method of reference to other sections of the book is clumsy (it is best to go via the list of contents) and it should be possible in a future edition to refer by page number. The treatment of ^{252}Cf as a neutron source is too brief (six lines), while Table

12.2 listing elements determined in various matrices would be usefully complemented by another table listed in order of matrix instead of element, although this is available elsewhere, for example, NBS Technical Note 467.

These, however, are relatively minor criticisms of a book which is sure to find an important place in any laboratory engaged in the field. H. W. WILSON

Transport Kinetics

Elementary Kinetics of Membrane Carrier Transport. By K. D. Neame and T. G. Richards. Pp. xii + 120. (Blackwell Scientific: Oxford, London, Edinburgh and Melbourne, 1972.) £3.

I SHOULD have liked to recommend this little book wholeheartedly. It is written in response to a definite need and the authors have successfully limited their treatment to the precise field of the title. There is, quite correctly, no discussion of the structure of membranes (although useful references are provided) and there is, again correctly, little on the properties of the "carriers". These entities are merely useful descriptions of experimental results and the book concerns itself only with the kinetic consequences of the carrier hypothesis.

The strength of the book lies in the really excellent sections dealing with the handling of kinetic data, and their analysis in terms of simple and complex carrier systems. The traps of too naive an analysis of the data and of too sophisticated an analysis of unreliable data are clearly pointed out. Most valuably, many of the examples used are wisely chosen and from a broad membrane literature, replacing the hypothetical examples that might have contented other writers. One necessarily anonymous provider of data and related "analysis" must be hiding his head in shame!

What a pity, then, that the sections dealing with fundamental theory do not match this high standard. Thus, for instance, the Michaelis-Menten equation is derived (in five laborious pages) in such a form that the concentration of binding sites appears in the Michaelis constant. The authors' terminology is often misleading, such as "association" and "dissociation" constants, where "on" and "off" constants would be more appropriate. Finally, the sections on exchange diffusion and counter-transport are completely misleading. An explicit experimental distinction between these processes has for a number of years been available. When William of Ockham (quoted by the authors in this context) wrote that "essences are not to be multiplied without necessity", he carefully included the latter words. W. D. STEIN

Insect Natural History

Insects of the World. By Walter Linsenmaier. Translated from the German by Leigh E. Chadwick. Pp. 392. (McGraw-Hill: New York and London, November 1972.) £6.50.

IN recent years there has been a spate of gaudy insect books richly illustrated with colour photographs; but in spite of the great technical improvements in colour film, in lenses, and in depth of focus, these books for some reason are apt to leave a feeling of dissatisfaction; and at the end of the day one turns with relief to the coloured copperplates of Maria Merian picturing the insects and other wonders of the tropics recorded during her journey to Surinam in 1699. Many of the same insects figure in Linsenmaier's book, depicted by hand in a different style but with something of the cornucopian extravagance that inspired Madame Merian's work. There is an abundant text, full of accurate information for those who care to seek it out. The text is illustrated by little monochrome vignettes, many of which bear a page and figure number where the same illustration can be found in full colour. The opening chapters provide simple outlines of anatomy and physiology, accounts of coloration, mimicry and camouflage, insect distribution and migration. But the main part is systematic. The insects are taken order by order, their description enlivened throughout by essays on every aspect of insect natural history. Finally, there are chapters on water insects and social insects—again systematically arranged and packed with information.

The book can therefore be read with interest, with the help of the thumbnail illustrations, without reference to the plates. But the plates themselves are fantastic, all 150 of them; and many readers will find it difficult to leave them and get down to the text. The vast majority are superb drawings of insects in the living state in their native haunts; often crowded together in some amazonian forest or palaearctic woodland so that the child-like entomologist can pore over them again and again, and still discover something he had not noticed before. Then there are plates of massed colour photographs of cabinet specimens figuring hundreds of the more or less conspicuous insects from most parts of the world. These are so good that many can be used for identification, or approximate identification, and by looking up the pages of small print at the end of the book their generic and specific names and country of origin can be found. Among the Lepidoptera the subjects range from *Nepticula* with a wing span of 4 mm to *Attacus* with a wing span of 36 cm! A spectacular book by a splendid artist who is an enthusiastic insect lover, well translated from the German by a distinguished American entomologist, L. E. Chadwick.

V. B. WIGGLESWORTH

EM *Vade-mecum*

Practical Methods in Electron Microscopy. Edited by Audrey M. Glauert. Volume I. Part 1. *Specimen Preparation in Materials Science.* By P. J. Goodhew. Part 2. *Electron Diffraction and Optical Diffraction Techniques.* By B. E. P. Beeston, Robert W. Horne and Roy Markham. Pp. viii + 444. (North-Holland: Amsterdam and London, 1972.) Dfl. 110; $34.50.

ELECTRON microscopy must be the interdisciplinary subject *par excellence*. The instrument itself is a relatively straightforward exercise in physics and electrical engineering, but its applications spread through practically all branches of pure and applied science, from concrete technology to macromolecular structure, from radiation damage in metals to the mechanism of muscular contraction. Further, having caught your rabbit, dissected, fixed, desiccated, stained and sectioned it into flakes thinner than one-tenth the wavelength of light, imaged it (in vacuum) in adequate illuminating conditions at a magnification up to ×300,000 and enlarged the micrograph yet further, there remains the crucial task of interpreting your results, of deciding what is "real" and what artefact in the multifarious details made visible. The metallurgist has a like problem in preparing his specimens and analysing his images of dislocations or precipitates, though these are less liable to artefact.

Twenty years ago it was possible, within the compass of 300 pages, to produce a fair survey of the subject, from the principles and operation of the microscope through specimen preparation to electron photography. True, the author (if solo) needed to be something of a jack of all trades to provide a reasonably balanced view of every topic, but the early electron microscopists had to be just that, serving as they usually did customers from various departments of a university or research centre. Even 7 years ago one man could still cope adequately with the *Elektronenmikroskopische Untersuchungs und Präparationsmethoden* in 600 pages (Springer-Verlag; 1967), although Dr Reimer had to rely on help and advice from numerous colleagues as the preface acknowledges. The French a few years earlier required two volumes totalling nearly 1,300 pages and a team of seven authors (*Traité de Microscopie Électronique*, Hermann, Paris: 1961), but gave more space to the microscope itself.

By the 1970s it is no longer possible to give an adequate treatment even within two such volumes. Quite apart from the natural spread of applications, major new instrumental developments continue to surprise us, such as the scanning transmission microscope, and new insights into image formation have allowed the heavier atoms to be "photographed". In this situation only a collaborative effort by a group of experts can do justice to the subject. A German scheme breaks it down into many small sections, which appear seriatim as each text is completed, to be bound in looseleaf form (*Methodensammlung der Elektronenmikroskopie,* Wissenschaftliche Verlagsgesellschaft, Stuttgart; 1971).

An English enterprise in rather different form has now been launched, edited appropriately by a physicist now researching in a biological laboratory. Dr Glauert is assembling a team of authors to provide a "comprehensive series of laboratory handbooks in which all the techniques of electron microscopy are described in sufficient detail to enable the isolated worker to carry them out successfully". The first volume certainly lives up to this aim. It has two parts, the first of which deals with specimen preparation in materials science. The chief preparative techniques for metals and other solid samples, including powders and fibres, are described by Dr P. J. Goodhew in 189 pages. Part 2 is in two sections, an introduction to electron diffraction by Dr B. E. P. Beeston (140 pages), followed by an account of the application of optical diffraction and image reconstruction techniques to electron microscopy by Professor R. W. Horne and Professor R. Markham (110 pages).

In selecting the authors the editor has obviously followed the rule enunciated in her preface that "it is not possible to describe a technique with sufficient practical detail for it to be followed accurately unless one is familiar with the technique oneself". Each contribution is well planned and clearly presented, starting from elementary principles and working up to the present state of the art. The text is illustrated with diagrams, charts and micrographs; references are given after each chapter and a list of suppliers of relevant equipment and materials at the end of each part. A subject index is also provided for each part, as the primary intention of the editor and publishers is for individual parts to be available in paperback form. In the same way volumes II and III are announced as each comprising two rather unrelated parts. So that what we are offered is a series of monographs, from which the advanced student or research worker can select those he needs on his work bench. The hardback edition appears to be provided mainly for the convenience of libraries. This is an imaginative venture which deserves to succeed, if the standard of the first two parts can be maintained. It is a little disappointing, however, that the price of the first paperback parts is still relatively high (about £4 and £5.50), almost two-thirds that of the bound volume I.

V. E. Cosslett

Peaceful Revolution

Management and Technology. Edited by Alan Mencher. Volume 1. An Anglo-American exchange of views. (Inforlink: Frimley, Surrey, 1972.) £3.80.

Will this be the "century of the mismatch", in which our technological power outstripped our strength of moral purpose, and our social institutions—designed for an earlier environment—proved unable to modify themselves quickly enough to tackle the right problems? Alan Mencher's selection from the discussions which he has so successfully organized at the US Embassy provides some answers. Blake, Ackoff, Ramo, Charpie, Schon and others—in talk and discussion with their British audience—show that the Americans have moved from the consideration of problems as isolated discrete issues to the position of studying them as part of the larger system which is their environment. They still lack the tools, concepts and experience for tackling complex systems problems but the systems approach, however imperfect, does force people to set down their goals and the criteria against which proposals can be judged.

Society, by creating an increasing need for a priority selection of satisfactions, is forcing political action and together these provide new opportunities for industrial endeavour. New ideas mean change, and rapid response to change may often only be achieved by revolution. The key problem in innovative management is how to produce peaceful revolution so that every individual's competence can be fully exploited. American business has reacted by, as Schon puts it, moving from the concept of a firm producing a highly aggregated product to that of the firm conceived as an organization built around a process as its defining character. This notion can best be seen in the constellation firm, such as 3M, in which semi-autonomous firms surround a bank and a development facility. Such a firm is highly adaptive—satellites can expand, contract or be replaced. Flexibility like this in industry imposes great strains on other institutions, particularly in research and education. These have to adapt to a faster internal rate of change, so that they meet more readily the real and continuing needs of firms and individuals alike.

One mis-match is very noticeable in this series of papers. These American notions of management have moved well ahead of ours. A contribution from a representative of one of America's beseiged or decaying industries would have introduced an interesting counterbalance, for not all would agree that rapid change is necessary or desirable. As we move closer into the European community, the clash of cultures in the problems of reconciling social and technological developments will become more devastating in their effect. The Americans have the advantage of being able to experiment on a larger scale than we can afford. Their search for solutions, as revealed in these papers, provides a valuable starting point for those of us who are beginning to recognize the nature of the changes in industry, government and educational systems which will occur during the rest of this century.

E. P. Hawthorne

Molecular Concepts

Atomic and Molecular Structure: The Development of Our Concepts. By Walter J. Lehmann. Pp. xix+449. (Wiley: New York and London, July 1972.) £5.50.

This book represents a courageous assault upon an important problem: how to teach aspects of a highly technical and mathematical science to people without a scientific background. In this case the subject is atomic and molecular structure and the students were those reading for non-science majors at Boston. Five main sections deal respectively with developments leading up to the periodic table, the evolution of the nuclear atom, elucidation of the electronic structure of the atom, quantum mechanics and molecular structure. One imagines the liberal arts students would turn often and gratefully to the appendices on the metric system and "a quick refresher on arithmetic procedures", to say nothing of the very full glossary.

The value of Professor Lehmann's work can only be assessed in practice, but it has the marks of sound educational strategy. Little is left to chance, the text is clear and interesting, there are some useful graphics, and self-assessment questions monitor the individual's progress. There are a few mistakes in formulae, equations and calculations, but they are not likely to be serious impediments.

In place of the conventional rigorous treatment of his themes the author adopts an approach that may be fairly termed quasi-historical. There is no attempt to give a complete historical coverage but each section has a broad historical framework. As he says, "we are interested in the logical development of ideas rather than tracing their history". Such an approach can be fraught with hazards, and it says much for the author that many of the most obvious pitfalls are avoided. Certainly we have Galileo at the Tower of Pisa, Newton's apple and a few other items from scientific mythology but these tend to be confined to the early centuries. More serious is the "whiggish" view of historical progress that is implicit in much of the book. The unfolding of science is seen as having "all the elements of a good detective novel" with "a solution of the mystery through sheer perseverance". But of the nonrational elements in scientific development, of the false starts and of the brilliant "hunch", little is said. This would not matter so much were it not the avowed aim of the book to emphasize how the scientist develops his theories and how he approaches a problem.

As a reliable historical guide, therefore, this book is inadequate. But it may well turn out to be a valuable companion to those concerned to communicate modern science within a nonscientific culture. C. A. RUSSELL

Unravelling Interactions

Migration of Interacting Systems. By L. W. Nichol and D. J. Winzor. Pp. x+166. (Clarendon: Oxford; Oxford University: London, November 1972.) £5.50.

BIOCHEMISTS classify electrophoresis, sedimentation and gel chromatography as migration processes. If these methods are used straightforwardly for separating biological macromolecules, only a relatively simple grasp of underlying principles is required, as long as the migrating material is confined to a thin zone. Nevertheless, this simplicity is paid for by a loss of information about macromolecular interaction, a matter of strong topical interest.

If the zone is made broad with a plateau of constant concentration intervening between its extremes, the conditions for interaction are preserved. Qualitative indications of interaction may then be obtained by comparing leading and trailing boundaries. Even at this level not much depth of theory is required. It is in moving to a quantitative measure of interaction that a new dimension of difficulty emerges.

In part this difficulty is inherent. Complexes have to be studied under conditions determined by the circumstances in which they are stable, ruling out such usual simplifications as extrapolation to zero concentration. Indeed, measurements have often to be made at sufficiently high concentrations for non-ideality factors to be dominant. Quite apart from this, very complicated effects of re-equilibration and diffusion within the boundaries need to be understood. Consequently a biochemist finds himself in the situation he has met before over X-ray crystallography and nuclear magnetic resonance spectroscopy, where he can feel himself diverted completely from his subject of study in order to master the tools needed to pursue it.

It is here that a monograph of the right kind could lead to a great economy of effort. Biochemists are likely to agree that for them this means one which begins at a very simple level with an account of the basic theory of interacting systems, but which then takes them step by step to a point where they are able themselves to deal with real systems.

The most recent advances turn out to be quite helpful in this respect, for much of the forbidding complexity of interaction theory has been due in the past to attempts to find analytical solutions of the basically simple flux equations. It is now quite obvious that all this can be by-passed and that answers of any desired precision will be obtainable by numerical methods without having to lose sight of the underlying physical situation and without having to neglect non-ideality factors, diffusion effects, pressure effects or any factors which can be clearly defined. A distinction can then be made between the initial very difficult job of writing the necessary computer programs to carry out the numerical work, and the subsequent use of these programs to analyse experiments.

This monograph does not adopt this point of view. In particular the introduction is very difficult for beginners to whom, after all, the editors address their monographs. Perhaps the authors felt that the well-known review article by Nichol *et al.* published in 1964 already provides a sufficient introduction. So readers have to do a great deal of hard work right from the first page, including mastering very general ideal cases of which a self-associating acceptor interacting with a self-associating ligand is a key example. One soon realizes that the book is patterned on the thirty or so papers written over the last ten years by the authors, and as they say in their preface, their choice of examples is "guided by the interests of the authors in protein research".

Even so, most areas of interest are touched upon, for example monomer-polymer systems in rapid equilibrium, and related "sigmoidal" ligand binding, protein–protein association and hybridization, protein interactions with buffer constituents, frictional effects and charge effects in sedimentation. Also considerable attention is paid to the quantitative side of gel chromatography in which the authors have played a prominent part. For those familiar with the subject, it is particularly useful to have an exposition summarizing the authors' point of view in a subject in which there remain many areas of controversy. One of these areas is clearly that of the effect of pressure on the sedimentation of myosin, for one notices that the authors' interpretation contradicts that of the American editor of the monograph who made the original discovery of this effect. G. A. GILBERT

Hormones on the Brain

Steroid Hormones and Brain Function. Edited by Charles H. Sawyer and Roger A. Gorski. (Proceedings of a Conference held in May 1970, California.) Pp. 388. (University of California: Berkeley, Los Angeles and London, 1971.) £13.50.

ABOUT fifty authors contribute thirty-two papers to these proceedings of a conference sponsored by IBRO and by the UCLA Brain Research Institute and Forum in Medical Sciences. The hormones of the book's title comprise those of the adrenal and gonads; brain function is appraised by electrophysiological and behavioural characteristics and elucidated by a variety of techniques including metabolic and histochemical ones and the placing of surgical lesions.

It is encouraging that in the brain, as in peripheral target organs, attachment has been found of steroid to cytoplasmic and nuclear components. W. E. Stumpf, basing his observations on the cerebral occurrence of oestradiol-binding proteins similar to those of the uterus, reports autoradiographic localization of the cells concerned. After systemic administration of [^{3}H]-oestradiol to rats, uptake was found to defined neurones of the diencephalon and amygdala, and not to glial and ependymal cells. It is suggested that the neurones concerned produced the pituitary secretions which in turn acted on the peripheral target organ. R. A. Gorski concludes, from implantation of actinomycin D in the hypothalamus of rats, that oestrogen action in inducing aspects of female sexual behaviour proceeds through RNA and protein synthesis. The RNA content of cerebellar explants is shown by A. Vernadakis to be increased by both cortisol and oestradiol, while B. S. McEwen describes excellently the differential localization of corticosterone and oestradiol in the rat brain.

In his "overview" of the conference,

J. M. Davidson queries how much of the behavioural effects of steroids occurs by action of the steroid at the brain itself—and answers: part only. With each well-investigated steroid, evidence was offered for direct action at the central nervous system, and further actions from peripheral organs. It is thus valuable that measurements can often be made in small quantities of blood of the relevant hormones. V. D. Ramírez describes determinations of luteinizing hormone and follicle-stimulating hormone in 0.2 ml. of plasma from rats by radioimmune assay.

The book carries prominently both behavioural and electrophysiological consequences of steroid actions in developing and in adult animals. Most papers are well-documented, but with figures awkwardly placed for consultation: not in the relevant text, but following it. Production and indexing of the book are good, and its discussion sections are plentiful and informative.

H. McIlwain

Fruit Fly

Drosophila. By Bryan Shorrocks. Pp. 144. (Ginn: London, October 1972.) £2.25.

Drosophila melanogaster is once again a popular beast in biological research laboratories, especially those devoted to developmental and biochemical genetics; it never did lose its popularity with the population geneticist.

This text by Dr Shorrocks will be useful to anyone starting to work with *Drosophila* since it provides a succinct and clearly written guide to general biology, laboratory culture, field ecology, methods of collecting, behaviour and elementary cytology. There is also a section devoted to elementary genetics with some suggestions for experiments suitable for the beginning student, but the most valuable single feature is the illustrated diagnostic key and ecological notes relating to a score or so of the commoner species found in Britain. It is ironic that even for species which have been widely used in genetic studies, little is known about their primary breeding sites, population sizes, fluctuations in numbers, distribution, and so on. The British fauna includes a group of closely related species like *subobscura, ambigua, tristis, obscura* and *subsilvestris*, whose population biology would certainly repay study. No doubt their similarity in appearance has hitherto often proved discouraging, but Dr Shorrocks's key and clear line diagrams have removed this obstacle and should stimulate comparative studies on the population ecology of these and other British species.

F. W. Robertson

Seeds

Seed Biology. Edited by T. T. Kozlowski. Volume I. *Importance, Development and Germination*. Pp. xiii+416. (Academic: New York and London, May 1972.) $26.40.

The first volume of *Seed Biology* is subtitled *Importance, Development and Germination*. It is part of a three-volumed work, the second of which will cover germination control, metabolism and pathology; the third will deal with applied aspects of the subject including insects, seed collection, storage, testing and certification. This first volume, then, is really meant to be seen as part of a larger work, and this is made clear by several references within its six chapters to material in subsequent volumes.

The whole work is introduced by T. T. Kozlowski (the editor) and C. R. Gunn in a short chapter dealing primarily with the significance of seeds in evolution, their great diversity and their importance to man. This is followed by two chapters on the development of seeds, concentrating mainly on anatomical aspects; H. Singh and B. M. Johri consider the gymnosperms and S. P. Bhatnagar and Johri the angiosperms. Both are worthy accounts which distil an enormous amount of information from a large number of references—nearly 350 in the case of angiosperms.

The fourth chapter by A. Fahn and Ella Werker is an interesting and straightforward description of the anatomical mechanisms of seed dispersal and, in spite of the large number of cases considered, they conclude that the principal types of device serving seed dispersal are quite small. The style and objectives of chapter 5 on the morphogenesis of seed germination by G. P. Berlyn contrast with the rest of the book. Instead of attempting an encyclopaedic coverage, the author has decided to take two contrasting genera, *Zea* and *Pinus*, and give a critical (and very readable) consideration which relates the anatomical and sub-cellular changes in seeds to the wider problems of morphogenesis.

Finally there is a chapter by B. M. Pollock and E. E. Roos on seed and seedling vigour. This is a wide-ranging account of a difficult subject—a difficulty which arises in part because of the lack of precision often attached to the term "vigour". Nevertheless, there are some interesting ideas here.

One cannot form a final judgment of a volume which is only one-third of a complete work, but there is little doubt that seed research workers will find it a useful reference book. Most chapters are designed primarily for a specialist audience, in spite of the publisher's blurb; it is unlikely, for example, that they will be of interest to seed growers, as is claimed. The production is very fine and the illustrations are good and lavish—and so they should be, considering the price. I shall look forward to seeing the subsequent volumes.

E. H. Roberts

Operational Research

Operational Research: Techniques and Examples. Edited by G. H. Mitchell. Pp. ix+275. (The English Universities: London, 1972.) £3.95.

This book is based on material used in the training programme of the Operational Research Executive of the National Coal Board, a programme now mounted jointly with Brunel University as a Master's Course, and follows the publication of a similar book[1] some ten years ago.

It contains chapters on all the major techniques associated particularly with OR: linear programming and its extensions, dynamic programming, decision theory and theory of games, networks, queues, stock control, replacement, and simulation. As such, it does not differ greatly from many other introductory books on OR, although the editor has managed to pack a lot of material into the 200 or so pages. Brief descriptions of many extensions of the basic techniques are given (for example, post-optimality analysis and parametric programming, decomposition, stochastic programming, separable programming, integer and mixed integer programming are covered in fifteen pages), together with further references, which will provide a good basis for an introductory course, but which will be tough going for the unsupported reader.

The editor has aimed to keep the mathematical level within the reach of anyone with "A" level mathematics, but the liberal use of algebraic notation is likely to make comprehension difficult for the reader who has not progressed beyond that level.

Each chapter is provided with a number of problems and worked answers, amounting to some fifty pages in total. The book is certainly a good candidate for selection as the main reference for an introductory course on OR.

Robert Harris

[1] Houlden, B. T. (editor), *Some Techniques of Operational Research* (The English Universities Press, 1962).

Addendum

In the bibliography to the review of the book, *The Careless Technology* (*Nature*, **240**, 268; 1972), the publisher was given as The Natural History Press: Garden City, New York. The book is also published by Tom Stacey, London.

CORRESPONDENCE

Coal

Sir,—In your article, "The Biggest Lame Duck of All" (*Nature*, **240**, 431 ; 1972), you make comments about the wisdom or otherwise of the measures now proposed for the British coal industry in the next few years. Your comments cover a range of topics from energy policy to the philosophy of control of the nationalized industries. These views will no doubt be given an appropriate place in the considerations of responsible individuals, including those who are concerned with the parliamentary stages of the Bill.

However, towards the end of the article, you ask why the new proposals have not been accompanied by some policy on research, a subject on which *Nature* would be expected to be well informed. I hope your readers will not be led to assume from this question that the National Coal Board lacks appropriate policies on research, especially in the field of future utilization technologies for coal. The Board's policy on research is not only a matter of prime concern to the Board itself but the appropriate Minister also has a statutory duty to satisfy himself that the research programmes of the NCB, along with those of other energy industries, are satisfactory. The Minister is advised on this by an advisory body having an eminent and expert independent Chairman and membership.

Furthermore, the Board has always made a great point of explaining its attitude to future developments in the role and modes of utilization of coal. Indeed the current Bill owes much to the growing acceptance not only that coal provides much the greatest reserve of fossil fuel but also that coal is capable of being used in a flexible fashion to replace other fuels, including liquid and gaseous fuels. The Board's research establishments are open to display the research work and to explain these policies. The laboratories have been regularly visited by numerous representatives of the press, government organizations, other related energy industries, and visitors from many countries. We have, incidentally, also made a point for a long time of presenting our proposed research and development programmes, before they are finally approved, annually to our National Consultative Committee, which is the representative body of our trade unions ; this body also visits our laboratories and takes a deep interest in the work. The Board's research work and policies have also been widely publicized through lectures and articles in both professional and popular journals. The consensus of international opinion certainly seems to indicate that the Board's current programme is sensible and that our longer range planning will allow us to develop our strategy as our opportunities expand, as we believe they will.

Nonetheless, the Board would still be willing to demonstrate its research work to *Nature* and to explain the reasons behind its policy. It would seem desirable that you should understand the facts before criticizing the policy of the Board, and indeed the Government, in this regard.

Yours faithfully,

L. Grainger

National Coal Board,
Hobart House,
Grosvenor Place,
London SW1

Developing Medicine

Sir,—The Cameroon Embassy would like to draw readers' attention to the fact that in addition to the training of highly qualified medical personnel (doctors, nurses, and so on), the University Centre for Health Sciences (CUSS) in Yaounde, Cameroon, also trains a large number of para-medical staff. In fact the CUSS complex is unique in Africa in that training involves all aspects of medical and sanitary sciences.

Nevertheless, the use of a large number of para-medical personnel should be and must be considered as a very temporary solution to health problems in developing countries. The ultimate aim is to have regular highly qualified medical personnel as soon as possible in as many medical and health centres as possible with the para-medical trained staff serving as complements to those centres.

In the colonial days, emphasis was laid on curative medicine only and well equipped hospitals and personnel. All these demanded a lot of money and technical assistance which was scarce in penurious developing countries.

The Government of the United Republic of Cameroon, aware of this situation, has reversed this policy and has rather laid more and greater emphasis and priority on preventive medicine. In this regard, in the current Five-Year Development Plan of Cameroon, priority has been given to the construction, extension and equipping of provincial hospitals ; quantitative and qualitative improvement of the training of medical staff ; development of preventive and curative medicine and a vigorous health education scheme for the masses.

The end result therefore would be the extension of health services, including all forms of medicine, to cover the entire population both urban and rural. This will include treatment, prevention, education, etc. It is intended to build 30 divisional and sub-divisional hospitals and to construct or develop 165 rural health centres in Cameroon

Thus the Development Plan of Cameroon is aimed at achieving equitable distribution and diversification of goods, services and human resources. Bilateral and multilateral aid is welcome but the ultimate goal is to drive towards self-reliance.

Yours faithfully,

Francois-Xavier Tchoungui

Ambassade de la Republic Unie du Cameroun,
Washington DC

Vietnam Bombing

Sir,—Your editorial on consequences of the bombing in Vietnam (*Nature*, **241**, 1 ; 1973) solves no problems but raises unnecessary puzzles of its own.

First of all, I cannot see how the hypothetical effect on the bombings on the coming Kennedy Rund of tariff reductions, or Dr Kissinger's dilemma (if it exists) in deciding between the White House and Harvard comes closer to "*Nature's* parish" than "The Vietnam war as such". Where, one wonders, can one find a reader of *Nature* who would not see more pertinence in questions such as "the long-term effects of the bombing, the use of CS and of herbicides and other methods of defoliation, both on the people and the ecology of Vietnam" which the AAAS now wants the National Academy of Sciences to investigate (see page 7 of the same issue)? For that matter, the lovers of nature I know would even take an interest in the short-term effects.

Secondly, where can we find the European statesman whom the "irrationality of the bombing over Christmas" has so boosted morally speaking that he felt free "to talk as an equal to the United States"? He seems spectacularly absent in the major European countries (England no exception), whereas Palme of Sweden and Jorgensen of Denmark have a prior record of not having needed that boost.

Thirdly, who among suffering mankind, other than Dr Kissinger himself, are you now prepared to take in as your parishioners?

Yours faithfully,

Morten Simonsen

The University of Copenhagen,
DK 2100 Copenhagen

Obituary

Sir Ronald Baskett

SIR RONALD BASKETT, who died on November 24, worked for almost the whole of his career in agricultural education and research. After graduation from Reading his appointment in 1924 as assistant to the Head of the Chemical and Animal Nutrition Division of the Ministry of Agriculture for Northern Ireland afforded him an opportunity to extend one of his important interests, namely, the application of the techniques of analytical chemistry to the study of the composition and nutritive value of foods for man and livestock. At Queen's University, Belfast, where he worked until 1959, he took part in early investigations of mineral metabolism of farm animals and on the quality of products such as bacon and eggs. This was at a time when agriculture in the province was becoming aware of the value of producer organizations in the marketing of produce and in the maintenance of quality so important to exporters to the mainland. Though at this time, and indeed subsequently in his career, he did not have much time to devote to his own research because of heavy administrative duties, Baskett succeeded in building up an enthusiastic group of research workers at Queen's which made considerable contributions to knowledge of the nutrition of pigs and poultry and the utilization of forage crops and the interest in these topics is still maintained in the Agricultural Chemistry Department.

He was appointed Head of the Chemical and Animal Nutrition Division in 1928 and Professor of Agricultural Chemistry at Queen's in 1935, helping in building up the Faculty of Agriculture and later acting as Dean for a considerable period. He had a great interest in course structures in agricultural science teaching and served as a member of the Inter-University Council for Higher Education in the Colonies. In 1950 he left Belfast to spend a two-year period as Agricultural Attaché to the British Embassy in Washington, returning to become Permanent Secretary to the Ministry of Agriculture in Northern Ireland, but he only remained in the post for a short period, returning to the University as Professor and the post of Chief Scientific Officer in the Ministry which he had held since 1947.

Baskett's long experience of university and government administration in science was of great value to him in 1959 when he undertook the onerous task of Director of the National Institute for Research in Dairying. Here he contributed greatly to the development of closer links between the University of Reading and the Institute. He recognized the value of these links in the applied sciences associated with agriculture. At Reading he took a particular interest in areas of research of immediate benefit to the dairy industry such as the development of husbandry procedures for the control of mastitis.

In addition to his day-to-day management of the Institute, Baskett also served on many committees, for example on milk composition and on the veterinary profession. He was Chairman of the ARC Working Party on the Nutrient Requirements of Pigs which published a report incorporating new recommended feeding standards for this animal in 1967.

He retired from the Directorship of the National Institute for Research in Dairying in 1967 and returned to live in Northern Ireland. It was a measure of his dedication to agricultural research that even after his retirement he was persuaded to undertake the Secretaryship of the ARC as a short-term appointment in 1971. During his year of office he took care of the negotiations between the Council and the Government Departments on science research policy and this work contributed greatly to the development of future arrangements for research management in this field.

He was awarded the OBE in 1947, received an Hon. DSc from Queen's University, Belfast, in 1963, and was knighted in 1966.

He is survived by his wife and three sons.

Errata

PARAGRAPH five of the News and Views article "Age and Cancer Incidence" (*Nature*, **241**, 238; 1973) described experiments in which tissue transplanted from cancer-susceptible animals into various hosts was found still to be cancer-susceptible when, long after the original operation, a carcinogen was applied to the transplant. Conversely, cancer-resistant tissue remained cancer-resistant even when transplanted into a cancer-susceptible animal. Unfortunately, the News and Views article inadvertently stated the opposite of this result.

IN the article "Terrestrial Heat Flow, the Neutrino Problem, and a Possible Energy Source in the Core", by V. M. Hamza and A. E. Beck (*Nature*, **240**, 343; 1972) the last figure in column 7 of Table 1 should be 0.71, and not 0.11.

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NATURE Volume 241 FEBRUARY 23 1973

Measured Sense on Pollution

SIR ERIC ASHBY has been the chairman of the Royal Commission on Pollution for the past three years and has frequently been criticized for not having used his position as a means of amplifying popular discontents about disposable bottles and other contemporary nuisances. His critics owe themselves the duty of reading his address this week to the Royal Society of Arts, one of the most moderate statements of what needs to be done and how it should be done, so far to have appeared. Whether the Royal Commission itself will and should long survive Sir Eric's impending departure—he retires at the end of the month—is doubtful. The need for the Royal Commission was, to begin with, a reflexion of the British government's wish to have some guidance as to how it should react to the great fuss that people were then making about the environment, and it has long since become apparent that British government departments are well equipped to take environmental problems in their stride. It would be much simpler if this were openly recognized, and if the exceptional device of a Standing Royal Commission were abandoned.

The theme of Sir Eric's lecture is that freedom from pollution costs money but that, in the present climate of opinion, people in countries such as Britain are prepared to pay quite substantial sums of money for clean air, clean water and public amenity. He argues that technological innovations must be assumed to have a positive social value in a first approximation, for otherwise they would not be taken up. But there follow a number of subsidiary questions to answer—are the side effects of technological innovation damaging to people and, even if they are not, may not society as a whole wish to be rid of these side effects? Sir Eric quotes the economists' view that everything would be simpler if the cost of technological innovation were included in the cost of manufacturing operations—one of the proposals canvassed but not adopted in the Royal Commission's third report—but goes on to describe how, at least in Britain, it may be more effective to persuade industrial enterprises to follow sensible courses; quoting the switch from stable to degradable detergents as an example. The fuss in the United States about the side effects of phosphates in detergents is, in his view, a cautionary tale. Fanned by public excitement and the mass media, the movement to ban detergents containing phosphates reached the point at which several states had adopted legislation on the subject and, by the beginning of 1970, Senator Edmund Muskie's subcommittee was expected to recommend a change of federal legislation enforcing a switch from hard detergents to materials based on nitrilotriacetate, but in no time at all Professor Samuel Epstein showed that the cure might be more dangerous than the disease. The moral is that public pressure is not an infallible guide to action. Sir Eric goes so far as to think that the legislation now being promulgated to restrict the emission from automobiles, in Europe as well as the United States, may be similarly injudicious—"I believe we and the Americans have over-reacted". And if it is a question of how best to spend money to reduce the side effects of the motor car, may it not be preferable to do something to reduce casualties from road accidents?

In his lecture this week, Sir Eric Ashby went on to deal with the complex of issues raised by Professor Dennis Meadows and his team of colleagues at the Massachusetts Institute of Technology. He appeared to accept the validity of the arguments of those like Professor Barry Commoner who have said that gross pollution is a product of the size of a population, its consumption of goods and services and of the amount of pollution produced per unit of goods and services, and acknowledged that the time must come when it will be insufficient simply to seek to control the degree of pollution per unit of output—steps will also have to be taken to stabilize population and to restrict consumption. But he has no patience with *The Limits to Growth,* chiefly because "it omits, deliberately or by mere oversight, known data which, if they had been included, would have given quite unsensational predictions about the prospects for the condition of man". As such, "it deserves the censure of scientists". But what if the assumptions had been correct and if the conclusions had been startling? Sir Eric acknowledges, as do all sensible people, that there is a need that society should be able to respond rationally to changing circumstances. Moreover, it is important that people should keep closely in mind the overriding truth that the case against pollution is not at present that the side effects of modern industry are known to be damaging but that there is a proper

Nature Index

The combined index for *Nature, Nature Physical Science* and *Nature New Biology* for 1972 will be available at the beginning of May.

The 1973 index will be available in January 1974. Thereafter, a two monthly index of articles which have appeared in the *Nature* journals will be included in *Nature* soon after each volume is completed. The annual index, which will still be published, will be more comprehensive and will include details of everything published during the previous year in the three journals.

Copies of the 1971 index, which was published at the end of last year, are still available from the *Nature* Subscription Department, Macmillan Journals Limited, Brunel Road, Basingstoke, Hampshire, at a cost of £1.00 or $3.00, postage paid.

wish among all kinds of people that freedom from nuisance, public amenity, is a commodity to be purchased for its own sake and for the benefit it will bring to later generations.

What does this imply for public policy, not merely in Britain but elsewhere? The first thing to be said is that because freedom from pollution must be regarded as a public good to be purchased with public funds, it is imprudent of societies to neglect to make comparisons with other kinds of public purchases—social security, education, health care and the like. One of the chief complaints against those who would have governments take draconian measures against polluters is that they have often neglected this comparison. Yet even in the affluent societies in which it is now understandable that people should put the purchase of public amenity high on the shopping list, there remain social needs of great importance which cry out for attention. In Britain, for example, investment in the National Health Service could well be held to be more beneficial than, say, further investment in clean air or clean water. To be sure, the choice is by no means clear cut, but the important point is that a choice of some kind must be made, at least if the government is at the same time required to pursue fiscal policies which minimize the manufacture of bank notes. The difficulty is that the population is rarely given a chance to make rational decisions for lack of sufficiently detailed and accurate information, which is why it falls to the government to guide discussion more firmly than in the past. Is it too much to ask that the British government should follow the American in providing the detailed costing of environmental policies which the Council on Environmental Quality has been publishing in recent years, and that it should also extend the techniques of cost/benefit analysis to other kinds of social investments with which improved amenity may be compared?

The question of how manufacturers and other enterprises which cause pollution should be regulated is also an economic question. Sir Eric Ashby is apparently persuaded that diplomatic negotiations between governments and polluters are sufficient, but such techniques are necessarily arbitrary. There is a tendency for governments to tackle the problems that can be tackled easily by administrative procedures and to let others slide away. In all the circumstances, it would be in the long run beneficial if some serious attempt were made to saddle polluters with the social costs which their activities entail—to internalize the externalities, as the economists are fond of saying. There are, of course, serious and almost philosophical problems in such procedures. Many people will protest that it is impossible to value numerically the absence of sulphur dioxide, for example, from the atmosphere. This, however, is too gloomy a point of view. There is no reason why governments should not operate a system of taxes which would, for example, be levied on such things as the total output of sulphur-dioxide from factory chimneys, with geographical variations from place to place designed so as to penalize most severely those who add to concentrations of pollutants which are already a nuisance. If governments were prepared to introduce taxes of this kind gradually, they would find that existing industries would not be seriously disrupted. At the same time, it would be possible to work towards a level of taxation which provided polluters with some incentive to be less of a nuisance and at the same time to estimate the consequences of the new taxation for the costs of their operations. What it would, of course, be necessary to avoid is a situation like that in which the government of Sweden found itself last year, when a proposal to levy a tax on disposable bottles turned out to be unacceptably expensive for consumers. But where major sources of industrial pollution are concerned, there is plenty of scope for constructive action so long as governments and their electors are willing to move gradually.

More Bad Science TV

THE complaint in *Nature* on February 2 (**241**, 300; 1973) that BBC television programmes have slipped into the bad habit of giving too much publicity to and too sympathetic an explanation of the irrational elements in modern science seems to have caused great indignation at the BBC. One member of the corporation, himself a distinguished and level-headed contributor to the corporation's broadcast output, said the other day that he and his colleagues would have protested in writing if the complaint were not so self-evidently wide of the mark. Others have said, with more justice, that a complaint like this should at least have acknowledged that the BBC has won a high reputation for itself in the presentation of vast themes in science to a popular audience by means of the outstanding television programmes jointly the work of Mr Philip Daly and Mr Nigel Calder, so that the redemption of the corporation's reputation for the level-headed presentation of science does not rely entirely on Dr Jacob Bronowski's impending series of programmes. Nobody will cavil about the high quality of these programmes, which are exceedingly distinguished but also, as it happens, infrequent—Messrs Daly and Calder manage one programme every eighteen months or so. And those who doubt the validity of the complaint that the majority of the BBC's routine science output on television is dangerously infected with heresy could do worse than look again at last week's Horizon programme, which came as close as any programme could to a celebration of irrationality.

The programme rejoiced in the title "Science is Dead—Long Live Science". It began with a re-run of some of the most gruesome of the gruesome films collected in recent years from Vietnam and with a facile and misleading analysis of the research and development budget of the United States government—what sense does it make to compare federal expenditure on military development with federal expenditure on basic research at universities without at least acknowledging that in the United States the bulk of civil development is paid for directly by the commercial companies who stand to benefit? It was entirely proper that the programme should have interviewed the two scientists originally responsible for the development of napalm and the defoliants which have been used in Vietnam, and that it should explain that both people are alarmed to see what use has been made of their research, but does it follow from that that science is dead? And even if it is the case that the United States forces in Vietnam had worked out ways of bugging the battlefields with hidden sensors, is there any rational case for implying, as the programme did, that the profession of science and not the political climate which made the Vietnam war possible is to blame? What those who devised this witless programme have done is to foster the entirely mistaken but popular belief that the Vietnam war would not have happened if it had not been for scientific research: there is, of course, an entirely valid case for saying that some of the horrors of the past few years have had their origin in the laboratories, but does anybody seriously think that there would have been no war if scientists had behaved differently or if the scientific community had been differently organized?

The rest of the Horizon programme was even more dangerously irrational. It is interesting that a scientist previously on the staff of the "national standards laboratory" (presumably a reference to the National Bureau of Standards) should have been so offended by FBI investigations of his political activities that he chose to resign and run a printing press instead, but the programme might have reminded those who saw it that there are many countries in which government employees are forbidden by their terms of employment to engage in any kind of public political activity and that there is a case for saying that scientists who dissent from government policies should not in any case elect to work in government laboratories. The Horizon programme also dealt with the notorious case of strip mining in West Virginia and with a young man who had given up his scientific career to battle against the bulldozers. But is it not simply bad reporting to fail to mention that one of the scandals of coal mining in West Virginia is that the operators are not required by law to restore the terrain they despoil (as they are in other parts of the world) and that one of the difficulties with which the environmentalists have to contend is illustrated by the way in which Mr Jay Rockefeller, who ran on an anti-strip mining ticket in the elections last November, was defeated presumably by the wish of the local population to put jobs before amenity?

The rest of the programme was largely an over-sympathetic account of a commune of young scientists who rejoice in the name "New Alchemists" and who appear to spend their time making windmills out of discarded differential gears, making compost and cultivating fish in tanks surmounted by greenhouses made with plastic strung across a geodesic dome. The commune's ambition appears to be the development of a life style that will provide a method of subsistence for similar communities when eventually the holocaust comes—and the Horizon programme used Dr Jonathan Beckwith not merely as an authority for saying when civilization will end but also as an excuse for alarming its audience with tales of genetic engineering. Quite apart from the muddled explanation of their activities which the members of the commune provided—the simple ecology of a fish tank was held to be incapable of objective analysis—the programme gave, no doubt by accident, a striking insight into the tendency of the New Alchemists to talk as if their secret knowledge would in due course allow them to ride omnipotently over the problems with which ordinary people contend. In the circumstances, perhaps, it is not surprising that they should have finished with a dash of Sun worship and the chanting of the strange word "Om" around a camp fire. If the objective of the programme's producers had been to analyse an interesting if familiar tendency for groups of people to see how far they can succeed in living without the appurtenances of modern civilization, it might have been useful, but the reporting would have had to be sharper and less reverential. What, in practice, they have succeeded in doing is to construct a programme that might better have been called "Science is Dead—Long Live Unreason". Those who wish to defend the BBC against the charge of being anti-scientific in the bulk of its popular television coverage should do something to explain how this disastrous programme came about.

100 Years Ago

NOTE ON A POLYDACTYLOUS CAT FROM COOKHAM-DEAN

BY the kindness of Dr. Plumbe, of Maidenhead, I have been able to procure one of these cats; and from the many curious points he possesses, I think a note on his peculiarities will interest some of the readers of NATURE.

Readers of Mr. Darwin's "Origin of Species" are familiar enough with the illustration he gives of correlation of arrest of development in the deafness of blue-eyed cats. Some years ago I showed that our great naturalist had fallen into error on this point, and that the correlation is not between the blue eyes and the deafness, but between the latter and the sex of the cat.

I have made a great many inquiries on this point, and have completely confirmed my former observation, that all perfectly white tom-cats are deaf, and that they have blue eyes occasionally, because that item of beauty is common among white cats. I have seen many white Tabithas with blue eyes, but none of them were deaf. My little "Pudge" from Cookham is perfectly deaf, and has one blue eye and a yellow one. For the first few days after I had him, I thought he could hear a little, but am now quite satisfied that his deafness is complete, though he is alive to sounds conveyed through solid media. A further point of interest is that he is not mute as most deafs are, but there is a kittenish shrillness in his voice and a loudness in his purring, which are not commensurate with his age. I think, therefore, that it is possible that early in life he may have heard a little, for I know of two instances where perfect mutism accompanied the deafness in cats, and I do not know of any contrary condition. The one yellow eye favours my view that "Pudge" may have heard in infancy his mother's voice. His sense of touch is extremely acute compared to that of another cat I have, but his sight does not seem so sharp as that of cats generally is. He has twenty-six digits, and these are arranged—seven on each fore limb, and six on each hind limb. The supernumerary digits on the fore limbs are thumbs, and are placed one on either side of the true pollex, being joined to it, but having no metacarpal bones. In the hind limb the supernumerary digit is probably of the same nature, or a supernumerary index, being placed on the outer side of the hallux, and attached to the tarsus by a completely-developed metatarsal bone.

LAWSON TAIT

From Nature, 7, 323, *February* 27, 1873.

Select Committee Picks up the Pieces

THE Select Committee on Science and Technology was taken aback last week when Mr Michael Heseltine, Minister for Aerospace and Shipping, appeared before it and announced that the government had decided to scrap the hovertrain project which Tracked Hovercraft Limited have been running for the past five years at a total cost of about £5 million. At that meeting he anounced that the company's work on linear motors would be continued through a joint arrangement between the National Research Development Corporation (NRDC) and Hawker Siddeley under which the government would subscribe £500,000 over four or five years and Hawker Siddeley £100,000. He also said that Tracked Hovercraft's work on magnetic suspension would be carried on by British Rail with the help of a £150,000 grant.

Later that same day he let it be known that there was a strong possibility that a joint company, involving the NRDC, Hawker Siddeley and British Rail, would be formed.

This week the select committee settled down to analyse the rights and wrongs of the decision and to decide whether or not it had been made at the right time. Appearing before it were members of the management of Tracked Hovercraft Limited and representatives of the company's staff association.

Fundamental disagreement with several of Mr Heseltine's reasons for cancelling the project emerged from the meeting. Mr T. G. Fellows, managing director of Tracked Hovercraft, criticized Mr Heseltine's view that there is no prospective market in Britain for the hovertrain, and that "the country would not tolerate the duplication of track" involved in building a hovertrain link between, say, London and Manchester. Mr Fellows pointed out that British Rail itself expected a capacity problem by the mid-1980s, when a British hovertrain might reasonably be expected to be a viable proposition, and would itself be "duplicating" track or looking for new routes altogether. As far as possible environmental damage is concerned, Mr Fellows said that a hovertrain track need not be completely elevated, but could be partly laid at ground level or in tunnels. And he added that noise gave "no grounds for concern".

Tracked Hovercraft also disputed Mr Heseltine's estimates of the journey time for a hovertrain on a route from London to Maplin Sands, the proposed site for the third London airport. Mr Heseltine had said that a hovertrain would take 36 minutes to do the journey whereas the company estimate a time of about 20 minutes. Mr Fellows said that as he had understood the views of the Department of the Environment, British Rail's Advanced Passenger Train would form the first link in 1980 and the hovertrain would supplement it in the 1980s or 1990s. It would serve both as a showcase and as the first of a series of inter-city links.

Members of the staff association took Mr Heseltine to task for his lukewarm attitude to the prospects of European cooperation on research into high-speed ground transport. In its submission to the select committee the association says that the European commission "is expected to approve before this April, a policy for a network of routes for Europe including Britain" and that the commission has recommended that European governments should engage in joint research into new transport media, notably tracked hovercraft. Mr M. R. Bailey contended that when Mr Heseltine had spoken of a lack of foreseeable demand in the home market, he had failed to take proper account of how bound up Britain now is with the rest of Europe.

Mr Fellows described what seemed to him to have been a change of heart within the Department of the Environment about the hovertrain at the end of last year. Before then, he said, there had been a good prospect of his company combining resources with British Rail to their mutual advantage. Mr Bailey suggested that because of the troubles with the Advanced Passenger Train, for example with the gas turbine propulsion system, the suspension system and the general structure, the Department of the Environment no longer has money available to fund the contracts which Tracked Hovercraft needed.

ENERGY POLICY

Robens's Solution

AN independent Energy Commission to advise the government on energy policy was called for this week by Lord Robens, former chairman of the National Coal Board and now chairman of Vickers.

Lord Robens said that the commission should be a permanent body staffed by experts in fuels economics and in the specialist technologies. It should undertake comprehensive long and short term studies and its remit should include coal, gas, electricity, oil and nuclear power.

"The commission, having no particular energy axe to grind would be able to objectively produce an energy policy, planned entirely in the national interest . . . the in-fighting between the publicly owned energy industries would cease, as their place in the energy pattern would be properly established".

The resources of the Department of Trade and Industry are totally inadequate to do the task, according to Lord Robens. Attacking the 1967 White Paper on energy, which he described as a miserable failure, Lord Robens pointed out that the civil servants responsible for it "are no longer there to face the consequences of its impotence". A permanent commission would be able to accomplish more than any *ad hoc* body.

Lord Robens, who was delivering the Potterton Lecture to the Institution of Heating and Ventilating Engineers, said that "without the slightest doubt, energy resources over the next ten years are going to be sorely stretched." He pointed out that "to an advanced industrial economy such as ours, the importance of secure energy supplies is out of all proportion to the cost . . . short term commercial price considerations should not be allowed to obscure the very real need for security of supply".

The commission would resolve the questions of who is to carry spare capacity and stocks, of how competition between indigenous fuels can be limited so the national interest is best served, and of how the commercial "rules" under which energy interests operate should be re-assessed in order to give a greater weight to long term considerations.

If the government struggles on to produce an energy policy from its own resources it will surely fail as miserably as it failed in the energy white paper of 1967, Lord Robens said. "Only an independent commission, in my view, would get the juxtaposition of coal, gas, electricity, oil and even nuclear energy about right".

SPACE

Plans for UK-6

PLANS for a UK-6 satellite to follow the Science Research Council's UK-5 are being drawn up. At present, UK-5 is the last of a series of scientific satellites that the SRC is financing; the launch is planned for late this year. But, although no firm decision has yet been taken, low cost, pre-project definition for a UK-6 satellite is taking place.

Three experiments are being considered for UK-6, the chief of which is being devised by Professor Peter Fowler and his group at the University of Bristol. The plan is to investigate heavy particles in the cosmic radiation, particularly those with atomic number $Z>70$. The design is unique and consists of a sphere 74 centimetres in diameter filled with a mixture of argon and nitrogen which scintillates when a charged particle passes through it. Within this sphere is a spherical shell of plastic 61 centimetres across in which Čerenkov light is emitted as a particle passes through. Information from both parts of the detector is necessary to pin down the charge of the particle and it is intended that both pulses of light will be detected by the same photomultiplier. A Čerenkov pulse of this kind has a spread of only about 20 nanoseconds whereas the scintillation takes about 70 nanoseconds to reach its peak and is about 300 nanoseconds long. The result is a double-peaked photomultiplier pulse. Information from the pulse can either be telemetered directly back to Earth or recorded on tape and relayed when the satellite is over Britain. The other experiments under consideration are two X-ray studies, one from the University of Leicester and the other a joint project between the Mullard Space Science Laboratory and the University of Birmingham.

The Science Research Council said this week that plans are at a very early stage and that approval for UK-6 to be built and launched has yet to be obtained.

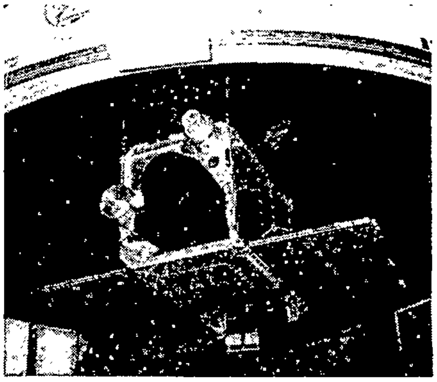
ESRO

TD-1A Wakes Up

EUROPE's largest and most expensive satellite, TD-1A, has been successfully reactivated after almost four months unplanned hibernation. Launched in March last year, the satellite is now to complete the ultraviolet and gamma-ray survey of the sky that was interrupted last November when the satellite entered partial eclipse in the northern hemisphere.

Originally the systematic star survey in the ultraviolet and gamma wavelengths was to be completed in the six months after launch. But in May the tape recorders on this, Europe's first astronomical satellite, failed, and provision was made to put the instruments into hibernation instead of closing them down permanently in case ESRO decided to continue the programme.

The hibernation procedure carried out in November is described as the most complex operation yet attempted by ESRO's operations centre at Darmstadt. Six hundred and eleven commands had to be carried through in 50 minutes without a hitch. Last week's de-spinning and reactivating of the spacecraft was carried out in stages from Tuesday to Saturday.



—*ESRO*

Structural model of TD-1A

Preliminary tests reveal that none of the instruments and sub-systems has suffered degradation during the shut-down, and the second scan may last until October 1973 when the craft will again enter eclipse. A period during May is particularly important as measurements that were lost last year when the tape recorders failed need to be repeated. When the second tape recorder on TD-1A failed in May, ESRO had to gather data in real time. At first only about 30 per cent of the data were being recovered on each orbit, but by the autumn, with the help of nearly 40 additional ground tracking stations, one of which was aboard a ship in the Pacific, this was boosted to about 60 per cent. Both NASA and the French CNES provided extra ground support. ESRO says that preliminary examination of the TD-1A data shows that approximately 50 per cent of the scientific work planned for the satellite was completed by last November. Seven stations have been added to the normal ESRO tracking network including Ahmedabad (India) and Mexico City. With these in operation, the second scan should increase sky coverage to about 85 per cent. Little has so far been published of the findings from TD-1A's seven experiments. The most striking results so far produced by the £8 million satellite have come from its largest experiment, the ultraviolet sky-scan telescope.

OECD

PCBs to be Controlled

THE manufacture and sale of PCBs are to be controlled. The OECD council decided in Paris last week that member countries may not use PCBs except for certain specific jobs where their non-flammability is essential. These include dielectric fluids for transformers, heat transfer fluids (but not in food and drug processing plants), hydraulic fluids in mining equipment and in capacitors. Otherwise PCBs may not be used either industrially or commercially.

Member countries will report to council in 1974, 1975 and 1976 on progress. Countries are encouraged in the council's decision to eliminate the use of PCBs as plasticizers pesticides, vacuum pump fluids, hydraulic liquids and heat transfer fluids (in the food and pharmaceutical industries), and companies are to be requested to use replacement materials "which are less hazardous to human health and the environment than the range of PCBs now in use".

Over the next three years OECD members are to exchange information on the amounts of PCBs manufactured, imported, exported and consumed and on the replacements for PCBs proposed by manufacturers. Methods of PCB disposal will also be discussed. Safety measures for containers and for transportation, a uniform labelling system and safe disposal systems are to be created by member countries.

The council's action follows mounting evidence that polychlorinated biphenyls are both toxic and persistent. Since 1966 when traces of PCBs were found in poisoned fish and wild birds, concern about the damage they cause has grown.

In 1971, a total of 48,400 metric tons of PCBs were produced in the OECD countries and concerted action by all the organization's members should do much to reduce the problem, because as far as OECD is aware, only its members actually manufacture PCBs in the western world.

In the long run the only use of PCBs that can be permitted, the council feels, is in large scale closed circuit long-life systems, which in effect means in transformers and in large capacitors. Recovery of PCB from these systems is practicable. In all other uses recovery is impracticable and the council wants these uses banned and suitable substitutes found.

The council is also eager that information on replacement products should be collected and reviewed. It would be ironic if, when replacements were in use, PCBs proved to be the lesser of the evils.

AEC Plans Peaceful Explosion but Raises Anger

by our Washington Correspondent

The Atomic Energy Commission has announced that it will soon set off an underground nuclear explosion in a remote area of Colorado in an attempt to free natural gas trapped in a deep layer of sandstone. The blast is part of a programme to test the feasibility of using nuclear explosives to extract natural gas from deposits which cannot be worked economically by conventional means. But, in addition to several million cubic feet of slightly radioactive gas, the explosion is likely to bring to the surface a good deal of bitter controversy.

If all goes according to the Commission's plan, three nuclear explosives, each producing a yield of 30 kilotons, will be placed in a vertical line, about 450 feet apart, in the gas-bearing sandstone. They will be fired simultaneously, and the blasts are expected to produce cavities which will join to form a huge cylindrical cavern some 150 feet across and 1,300 feet high, filled with broken rock. The blasts will also smash the surrounding sandstone, releasing natural gas which will then flow into the cavern. The idea is to keep the gas sealed in the cavern for several months to allow short lived radioisotopes to decay. Some of it will then be brought to the surface, its radioactivity will be measured and it will be burned.

Called Rio Blanco, after the Colorado county in which it will take place, the test will be the third and the largest in the AEC's gas stimulation project, which is all that now remains of the Plowshare programme—a venture conducted jointly by the AEC and industry which is designed to find peaceful uses for nuclear weapons technology. The project may eventually lead to commercial production of natural gas by nuclear blasts, but at this stage it is entirely experimental.

The justification for going ahead with Rio Blanco, according to the AEC, is that all-embracing catchphrase "the energy crisis". Because natural gas contains very few pollutants, it is becoming more and more desirable for a variety of uses, but there is estimated to be only about 12 years' supply in workable deposits in the United States. In a deep layer of sandstone underlying the Rocky Mountain area, however, there is reckoned to be at least another ten years' supply but because the sandstone is relatively impermeable, just sinking a well will not release enough gas to make the effort worth while. Hence this attempt to make the sandstone more porous by smashing it up with nuclear explosives.

The Rio Blanco shot itself will be fired off sometime after March 31, in a sparsely populated region of Colorado called the Piceance Creek Basin. Although the AEC is at pains to point out that the test does not imply that there will definitely be further explosions in the area, if Rio Blanco is judged a complete success—the gas yield, radioactivity and structural damage caused by the seismic shock will all be taken into consideration—it would be followed by four or six more tests a couple of years later. The third and final testing stage would be a pilot programme

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AUTO EXHAUSTS

Standards in Doubt

by our Washington Correspondent

A COMMITTEE of the National Academy of Sciences reported last week that automobile manufacturers should be capable of producing automobiles by 1975 which meet the stiff emission control standards specified by the Clean Air Act. But its conclusion also carried some severe qualifications, and the committee is much more equivocal about the manufacturers' ability to produce cars which meet the even stiffer requirements for 1976 models. The Clean Air Act specifies that 1975 model cars must emit 90% less carbon monoxide and hydrocarbons than 1970 models and that by 1976, emission of oxides of nitrogen should also be cut by 90% when compared with 1971 models.

The NAS committee reported that four types of engine seem likely to meet the 1975 standards — conventional engines equipped with catalytic converters, the Wankel engine equipped with an exhaust thermal reactor, the diesel engine and the new carburetted stratified charge engine which is being developed chiefly in Japan. But the committee also believes that there must be provision in the act for one change of catalytic converter in the 50,000 durability testing and that for all the engines, emissions must be averaged during the tests. If these qualifications are allowed, the committee believes that the technology is available to meet the 1975 standards.

As far as the 1976 standards are concerned, however, the committee reports that although five different systems have been tested successfully at low mileage, all have failed after a few thousand miles, and there is considerable doubt about the manufacturers' ability to mass produce engines to satisfy the demand. The most promising engine to meet the 1976 standard seems to be the dual-carburetted stratified charge engine, which now seems to be cheaper, more dependable and more economical to run, but it is unlikely to be as readily available as conventional engines with a dual catalyst system. These conclusions have led the committee to warn that the American automobile industry seems to be putting most of its eggs into one basket by concentrating on catalytic converters, but the stratified charge system seems the best bet in the long run.

In a letter transmitting the report to Congress and to the Administrator of the Environmental Protection Agency, Dr Philip Handler, president of the National Academy of Sciences, points out that the cost of catalytic converters, combined with the extra costs associated with loss of mileage per gallon because of the emission controls, add up to a total annual expenditure for emissions control of about $2,700 million. This cost, he suggests, should be carefully weighed against the benefits, and its effect on such factors as GNP, balance of payments and so on should be carefully studied. In particular, he suggests that attention should be paid to the possibility of enforcing the emissions standards only in those areas "where air quality is known to be adversely affected by automotive emissions", and reserving national implementation until more reliable and less expensive emission control devices are available.

Automobile manufacturers have always maintained that emission control technology will not be available in 1975 to meet the standards imposed by the Clean Air Act, and they requested one year's delay in implementation of the controls. After a lengthy public hearing, however, Mr William D. Ruckelshaus, Administrator of the Environmental Protection Agency, denied their request. But a few days before the NAS committee published its report, a federal appeals court directed him to reopen the hearings.

in which between 20 and 60 wells would be blasted out to produce sufficient gas to justify a major pipeline. Complete development of the Rio Blanco gas field would entail stimulation of up to about 300 wells.

The test will be the first to employ several explosives, and it will also use a new explosive device designed to produce a low yield of volatile radioactive isotopes, particularly tritium. Two previous explosions in the gas stimulation project, called Gasbuggy and Rulison, produced gas yields between five and ten times higher than would be produced by sinking a single borehole into the sandstone layer, but the gas was too heavily contaminated with radioactivity to be used commercially.

The chief objectives of the Rio Blanco test are first to measure the improvement in gas yield by using multiple explosives and, second, to see whether the new device can cut the radioactivity down to an acceptable level. Another part of the experiment will be to remove water and also tritium from the gas and to re-inject these products into the ground through a second borehole. If that manoeuvre is successful, the radioactivity in the gas would be approximately halved. Once brought to the surface, the gas will be burned in the atmosphere. If the water cannot be re-injected into the ground, it will simply be fed back into the gas stream and vapourized.

The project could ultimately lead to the commercial production of natural gas containing small quantities of radioactivity, and there is certain to be strong opposition from environmental groups. The AEC reckons that if nuclear stimulated gas is used for domestic purposes, a user could be exposed to less than an extra 1 per cent of natural background radiation, but there is also a chance that the explosions will cause structural damage to buildings in the area. Several organizations last week said that although they are vehemently against the project, they have so far no plans to try to stop at least the Rio Blanco test.

The most bitter opposition is likely, however, to come from the oil industry. The Rio Blanco gas deposits lie directly underneath what is believed to be the richest oil shale field in the world, and several oil companies are lining up to bid for rights to develop the field. They believe that their operations could be hurt by Rio Blanco, and that they could be completely devastated if the gas field were ever fully developed commercially. The Department of the Interior is planning to lease oil shale fields in Colorado, Utah and Wyoming to oil companies, and is at present preparing a final environmental impact statement on the proposed leasing. The impact statement should be ready in a few weeks, and leasing could take place a month after its publication—just at the time when Rio Blanco is due to be fired.

Oil shale developers are worried that gas stimulation blasts in the Piceance Basin may fracture the oil shale strata, which would make mining more difficult, that they would collapse the mines themselves and that they would damage the retorts on the surface which are used to distil oil from the shale. Partly for these reasons, officials in the Department of the Interior and also the governor of Colorado, Mr John A. Love, have been lukewarm or even opposed to the gas stimulation plans for the area. But they have somewhat reluctantly given their consent to Rio Blanco, although their support for any further blasts in the area cannot be guaranteed. Mr Rogers Morton, Secretary of the Interior, and Dr Dixie Lee Ray, the new chairman of the Atomic Energy Commission, have jointly given assurances that the Rio Blanco test will not damage the oil shale fields.

The oil companies point out that the Piceance Basin contains an estimated 500,000 million barrels of oil, which would contribute considerably more to solving the energy crisis than the natural gas which is likely to be derived from the area. The royalties which they would pay to the state of Colorado from development of the oil shale are also likely greatly to exceed any royalties from the production of gas. Asked last week whether legal action is likely to be taken to try to prevent Rio Blanco taking place, an executive of one interested oil company said that "we will continue to oppose this project and we shall have to decide what action will be necessary".

Apart from the oil companies, some residents of Colorado are not happy about the Rio Blanco test and the developments which may follow from it. They are worried about two chief consequences—seismic damage from the blast and radiation exposure. In an environmental impact statement published in April last year, the AEC estimated that Rio Blanco would cause about $50,000 worth of damage to buildings in the area, and the commission is recommending that work be suspended in mines nearby and that some buildings be evacuated.

A spokesman for the Colorado branch of Environmental Action pointed out last week, however, that the AEC predicted in 1969 that the Rulison blast would cause no seismic damage at all, but eventually ended up by paying out about $100,000 in damages. "We just can't trust what the AEC tells us", he said. Moreover, if a single test is estimated to cause $50,000 worth of damage, what will be the effects of complete development of the field with some 300 gas stimulations?

The AEC points out, however, that it is developing a technique for setting off explosives in sequence instead of simultaneously. The idea is to wait for the seismic shocks from one explosion to dissipate before setting off the second, and so on. This scheme would mitigate the seismic effects because the individual explosions would be much smaller, but the problem is that the explosive devices must be sufficiently rigged so that the blast from one will not affect the others. The AEC was, in fact, hoping to test sequential firing in Wyoming in 1974 in a test codenamed Waggon Wheel, but the 1974 budget for Plowshare has been slashed considerably and no money has been provided for the test. The earliest possible date for Waggon Wheel is now reckoned to be 1976.

As for radiation exposure, the chief source of radioactivity from the Rio Blanco test is likely to be flaring the gas at the wellhead, the most predominant radioisotope being tritium. The AEC's environmental impact statement suggests, however, that the maximum dose received by local residents will be less than 1 per cent of the background radiation in Colorado. The AEC is also sure that since the test will take place at about 6,000 feet beneath the surface, it will not contaminate groundwaters with radioactivity.

But Dr H. Peter Metzger, a Coloradoan who has recently published a book about the AEC (*The Atomic Establishment*, Simon and Shuster, $8.95), sums up the fears of local residents by suggesting that if the gas field is fully developed, "the chances are that sooner or later the wastes will contact an underground water supply and, through fractures, be brought to the surface and enter the biosphere". This suggestion is hotly denied by the AEC.

Perhaps the chief criticism of the gas stimulation project is simply that it is bad technology. Several of the opponents of Rio Blanco said last week that they seriously doubt whether the nuclear gas stimulation will ever be used commercially because of the possible environmental effects and also because consumers would be unwilling to use gas contaminated with radioactivity, even at the minute levels which the AEC is predicting.

Why is the AEC so keen on the gas stimulation programme, in spite of the opposition to it? One reason is that the programme is all that is left of Plowshare. Once a grandiose scheme for using nuclear explosives for all sorts of wierd and wonderful projects, such as excavating harbours and canals, Plowshare has been forced underground because of the radiological consequences of setting off nuclear blasts in the atmosphere—not to mention the test ban treaty. And Metzger also suggests that the gas stimulation project is particularly interesting to industry because of the potentially large work volume involved (Rio Blanco is being conducted in conjunction with a company called CER Geonuclear Corporation). But the project's trump card is clearly the energy crisis.

ENVIRONMENT

Nixon's Plans

by our Washington Correspondent

LAST week President Nixon sent to Congress a message outlining his Administration's plans to clean up and protect the environment. The message was accompanied by a package of bills and by some sharp criticism of Congress for foot-dragging on key environmental legislation. But soon after the message was received on Capitol Hill, Senator Edmund S. Muskie, who has long been at odds with the Administration over environmental matters, erupted with a statement of his own in which he lambasted Nixon for being long on rhetoric but short on commitment to environmental quality.

Claiming that the Administration is "well on the way to winning the war against environmental degradation—well on the way to making our peace with Nature", Nixon sent to Congress some 22 bills, 19 of which are reformulations of bills which were introduced last session, but which either languished in committees or got lost in the backlog of legislation awaiting final action when Congress adjourned for the elections.

A chief aim of the Administration's environmental plans is the development of policies for better use of the land—the proposals submitted to Congress last week include a new power plant siting law which sets out procedures for public review and comment, a measure to protect coastal wetlands and a new bill to regulate strip mining more closely. Other bills include a proposal for regulating toxic substances, a tax on industrial plants which emit sulphur oxides in regions in which the primary air quality standards are not being met, and a sheaf of legislation designed to protect wildlife.

Muskie is upset not because the Administration is proposing all these bills, but because he feels that it is not moving forcefully enough in implementing legislation which has already been passed. He is, of course, particularly irked by the fact that Nixon tried to veto the Water Pollution Control Bill last year, and when his veto was overridden, announced that he would not spend more than half of the money which it authorized. In the light of such action, Muskie says that he is "amazed that the President expects us to believe that under his leadership the Federal Government will 'play an active, positive role' ".

Among the new initiatives proposed in the Administration's package of bills are the following:

- The Administration will again ask Congress to provide authority for states and local governments to use highway trust funds for the development of mass transit systems. The Highway Trust Fund consists of special highway taxes which at present can only be used for building and improving highways, but Senator Muskie has already introduced a bill aimed at changing the law so that the funds can be tapped for mass transit systems. Although the Administration has supported such moves in the past, Russell Train, chairman of the Council on Environmental Quality, said last week that President Nixon now considers it "one of the highest priorities for action this year". The bill is, of course, being opposed by the so-called highway lobby—motorist organizations and construction companies which have consistently argued that the solution to the United States' transport problems is to bury more of the country under concrete.

- New legislation has been introduced which would give the Administrator of the Environmental Protection Agency power to establish safe standards for drinking water. Water suppliers would be required to notify customers whenever the standards are not met, and although the states would retain the chief enforcement powers, the Federal Government would step in if a hazard seems imminent.

- The sulphur tax proposal is being reintroduced this year, after a thorough review within the Administration and in spite of the fact that it has little support within the House Ways and Means Committee, to which it will be referred. Late last year, it seemed likely that the proposal would be dropped because of the shortage of low-sulphur fuels, but the Administration now believes that the technology for scrubbing stack gases will be available by 1976, a year after the primary air quality standards must be met. The proposal is to levy a tax of 20 cents per pound of sulphur emitted and the tax would come into effect in 1976 only in those areas in which the primary air quality standards—which are designed to protect health—are not being met. In addition, the Administration is proposing that the tax should be imposed in 1979 in those areas in which the secondary air quality standards—which are designed to protect vegetation, property and aesthetic values—are not being met. The idea is to provide an extra incentive for companies to clean up their smoke stacks and also to force low-sulphur fuels to be allocated to regions where they are most required.

Although the message and the package of bills provides a blueprint for the Administration's environmental policies, a more important message in this area will be submitted to Congress in the next few weeks. It will be President Nixon's long-awaited message on energy policy, in which he is expected to outline plans for meeting the energy crisis. The environmental impact of such plans—for example, he is expected to recommend increased use of coal—will be watched closely, but of more far reaching import will be the Administration's revised plans to revamp the federal bureaucracy along functional lines. One of the proposals will be the creation of a Department of Natural Resources, but exactly what such a department would contain is still an open question. The environmental message made no mention of bureaucratic reorganization, and it is now expected to come with the energy message.

Short Notes

Technology Assessment Board

Now that the House of Representatives has finally got round to sorting out its committees for this session, the board of the Office of Technology Assessment has finally been appointed. It was announced recently that Mr Olin Teague has been appointed to take the place of Mr Earle Cabell, now departed from Congress, and that Mr Morris Udall of Arizona will take the place of Mike McCormack, who has relinquished his place on the board because of his commitments on the new subcommittee on energy.

HEAO

WHAT is left of the High Energy Astronomy Observatory programme, already a casualty of budget cuts (see *Nature*, **241**, 83 and 306; 1973), may now be a pawn in further political moves. Originally envisaged as a very large automatic observatory, HEAO has been deferred while attempts are made to find ways in which some of the original objectives could be achieved more cheaply. The obvious way to do this would be by a continuation of the Orbiting Astronomical Observatory series, with which the Goddard Space Flight Center has now achieved a degree of success, notably with Copernicus (OAO-C). But if rumours now circulating are to be believed, the rump of the HEAO programme will be taken over by the Huntsville team who have great experience of developing large rockets (such as Saturn) but none of scientific satellites. The reason for the switch? To avoid embarrassing layoffs at Huntsville, now there are few big rockets wanted.

NEWS AND VIEWS

Does Polar Wandering Occur?

WHEN the few palaeomagnetists of the early twentieth century discovered that the directions of the ancient geomagnetic field, as derived from rocks, apparently differed from the direction of the contemporary field, two principal explanations were open to them. The first was simply that the results were not what they purported to be. To most scientists of the day, the idea that a rock could record the direction of the ambient field at the time of its formation, and that the record could maintain its stability over millions (or even thousands of millions) of years, must have seemed quite preposterous ; and this no doubt accounts, in some part, for the fact that palaeomagnetism attracted very little serious attention until the late 1940s and the early 1950s. It is one of the ironies of scientific history, of course, that the first palaeomagnetists were working almost exactly at the time that Wegener was proposing continental drift. Continental drift was not readily accepted either, although for different reasons ; and it is interesting that the chief conceptual objection to drift (the lack of viable mechanism) was overcome some forty years later just as palaeomagnetism was providing convincing evidence that drift had in fact occurred.

The second explanation occurring to the pioneers of palaeomagnetism was that the results reflected a true difference between the past and contemporary fields ; and as the early workers had hoped that palaeomagnetism would provide information about the ancient field, this positive explanation proved the more attractive. Lack of systematic data precluded anything more than the general conclusion at this stage ; but by the early 1950s it had become clear not only that the past and present fields apparently differ but that the difference has some sort of systematic relationship with time. For a brief period the more detailed results seemed to be consistent with the idea that the geomagnetic pole had moved with respect to the geographic pole. This was (geomagnetic) polar wandering in its most basic and literal sense. It is worth noting, however, that ancient geomagnetic poles were derived from palaeomagnetic data on the assumption that the field has always been dipolar. Thus an hypothesis that some of the early workers had set out to confirm or refute (the very existence in the past of a pair of geomagnetic poles) now appeared as a basic assumption, although it was not inconsistent with the data derived from rocks.

In so far as an historical thread is discernible among the rapidly changing concepts of the period, the next, practically simultaneous, step was the proposition of the first, and so far only, viable theory for the origin of the geomagnetic field—that the field results from motions in the Earth's fluid core. Because such motions must be governed in part by the effects of the Earth's rotation, one consequence of the core origin theory is that the geomagnetic axis must, on average, lie along the rotational axis, the only unique axis in the Earth (although, in practice, the geomagnetic axis appears to oscillate about the rotational axis with a standard deviation of about 11°). Thus it became apparent that the ancient geomagnetic pole could not have wandered from the geographic pole to the extent demanded by the palaeomagnetic data. This placed palaeomagnetists in a dilemma which was soon resolved by the realization that the same effect could be achieved if the whole Earth had moved relative to the axis of rotation (now conceptually locked to the average geomagnetic axis). If the Earth as a whole slips with respect to the rotational axis (which remains fixed relative to the Sun, apart from precession and nutation), it is clear that a rock becoming magnetized will not be able to distinguish between such a slip and a wandering of the geomagnetic pole from the geographic pole. The movement of the whole Earth relative to the rotational (geomagnetic) axis is now termed true polar wandering or simply polar wandering. A variant of it, which would achieve the same palaeomagnetic effect, is a movement of the crust (or lithosphere) as a whole with respect to the rotational axis. In this case the mantle could be regarded as fixed relative to the rotational axis with the crust (lithosphere) sliding over it as a single block or shell.

But one of the consequences of polar wandering is that all rocks of the same age that give a valid palaeomagnetic result at all should lead to the same position of the ancient geomagnetic pole, irrespective of where on the Earth's surface they acquired their magnetization. It soon became clear, however, that this consequence was not confirmed by observation. Although each continent seemed to have a relatively simple polar wandering path with time, the paths were different for different continents, at least for about the past 200 million years. The only possible explanation for this, assuming the field always to have been dipolar, is that continents have not only moved relative to the poles but also relative to each other.

Continental drift during about the past 200 million years (Wegenerian drift) is now almost universally accepted. But at this point it may be asked to what extent the measured continental motion is continental drift *per se* and to what extent polar wandering is also involved —in other words, is all the measured movement of continents strictly relative movement or is there also a component of non-relative movement caused by the rotation of the whole Earth or crust (lithosphere) with respect to the rotational axis?

This is not an easy question to answer. It is not difficult to distinguish palaeomagnetically between polar wandering and continental drift if one or the other acts alone ; but if drift and wandering occur together, the drift effectively obscures the wandering. Because the only available frame of reference in the Earth is the rotational axis, combined drift and wandering is mathematically (and palaeomagnetically) indistinguishable from drift, whatever may have happened mechanically. It is for this reason that polar movements derived from palaeomagnetic data are often referred to as apparent polar wandering. Thus apparent polar wandering can represent relative motions between continental blocks (continental drift), a component of motion common to all continental blocks (polar wandering), or a combination of the two.

So how can polar wandering, if present, be detected in a continental drift situation? Duncan *et al.* (*Nature*, **239**, 82 ; 1972) recently attempted to do it, making use of the mantle plumes postulated by Morgan (*Nature*, **230**, 42 ; 1971). They assumed, first, that mantle plumes are fixed relative to the mantle, and second, that igneous activity not associated with plate boundaries is a consequence of the surface effects of plumes, bands of igneous activity being caused by the passage of lithospheric plates over the mantle-fixed plumes. There are dangers here, of course. For one thing, plumes may not exist, and even if they do the two assumptions may not be valid (as Duncan and his colleagues freely admit). But the attractive conceptual point is that the fixing of the plumes to the mantle gives an absolute frame of reference which, in theory, enables polar wandering to be separated mathematically from continental drift. If polar wandering alone takes place by a rotation of the whole Earth with respect to the rotational axis, a mantle-fixed plume will also remain fixed to a continent or lithospheric plate. If, however, continental drift (or lithospheric plate motion) occurs, a plume trace will be produced as the continent moves over the plume. The continental drift proper may then be derived from the plume trace and subtracted from the apparent polar wandering (continental drift plus polar wandering) to give the true polar wandering.

By analysing the igneous activity (assumed plume traces) in the Central Volcanic province of Europe and the Thulean province of Iceland, the Faeroes and the British Isles, Duncan *et al.* concluded that plume and palaeomagnetic data are only consistent if true polar wandering of about 23° has taken place since the lower Tertiary. But on page 523 of this issue of *Nature*, McElhinny concludes independently that during the past 50 million years the lithosphere as a whole has not slipped significantly with respect to the rotational axis. The two conclusions are clearly incompatible. At this stage the most reasonable inference must be that plumes, if they exist, cannot be fixed to the mantle, although it may also be overenthusiastic to regard every volcano as a hot spot.

P. J. S.

Stratospheric Molecules

THE development of supersonic airliners has renewed interest in the chemical composition of the stratosphere. In particular there has been a lively debate about whether the passage of such an aircraft through the stratosphere will initiate changes in the chemical balance. The projected cruising altitudes of Concorde and its Russian rival are much lower than the ozone layer, and are therefore much less liable to deplete it than the supersonic airliner proposed in the United States in 1971. Another source of changes in the composition of the stratosphere has been the programme of nuclear tests, which may possibly have depleted the ozone shield by 5 to 7 per cent by causing the injection of nitrogen oxides. The result of this interest has been an expansion of studies of the upper atmosphere, particularly by spectroscopic methods, which are less susceptible to local contamination by the observation system. By combining data collected from various observation platforms, such as aircraft, balloons and satellites, it is gradually becoming possible to chart the global distribution and vertical distribution of the important chemical constituents of the atmosphere.

Recent work by Harries, reported on page 515 of this issue of *Nature*, predicts some useful data on the world-wide distribution of some of the important chemicals found in the stratosphere. Measurements of the submillimetre far-infrared emission spectra of the stratosphere were made from Concorde 002 during the tour of the Far East in June 1972. The analysis of the spectra has provided concentration data for water vapour, ozone, nitric acid, nitrous oxide, nitrogen dioxide and sulphur dioxide. Many of these compounds can be produced during fuel combustion, and their formation at much lower altitudes was mentioned in *Nature* recently (**241**, 341 ; 1973). Harries's preliminary study indicates that there are no significant variations of the chemical composition with latitude, but the results suggest that the vertical distribution, particularly for nitric acid, may well be non-linear. The concentrations of water and ozone measured in this way are of the order of 4 parts per million above the tropopause, which was generally at an altitude of between 40,000 and 50,000 foot. Nitrous oxide, an important link in the nitrogen cycle, has a concentration about 10 per cent of that of water in this region. Nitric acid, nitrogen dioxide and sulphur dioxide have much lower concentrations which are about 0.1 per cent of that of water.

The results that have been obtained so far, averaged over altitude, tropopause height, and location, do not reflect any of the known seasonal trends. It is known that the ozone concentration does vary with time and location, and it would be interesting if the present experiments could be extended to more southerly latitudes than 40° S to see whether there is any polar increase. Some of the other species of interest, such as nitric acid, are thought to be associated with ozone, as suggested by Murcray *et al.* (*J. Opt. Soc. Amer.*, **59**, 1131 ; 1967), and so may well exhibit similar fluctuations. Some transient species such as NH and NH_2 have probably been identified in the stratosphere by their electronic spectra, but their concentrations are unknown. Measurement of their pure rotation spectra would enable good estimates to be made of their abundance, for their dipole moments are either measured (in the case of NH), or estimable (in the case of NH_2).

Further experiments in this series should provide data which may answer some of the questions posed above, and may allow vertical concentration profiles to be derived for various localities. The information gained from this and similar experiments at varying altitudes should lead to the construction of an improved model for the chemical processes in this region.

From a Correspondent.

Synthetic Hepatitis B Vaccine?

CONSIDERABLE efforts are currently being directed towards passive and active immunization against hepatitis B infection. There is some evidence that passive immunization, using gamma globulin prepared from plasma containing high titre antibody to hepatitis B antigen, offers significant, though temporary, protection against infection. Trials with heated whole serum containing hepatitis B antigen have been carried out in New York (see *Nature*, **233**, 92; 1971) and more recently in Paris. Heat-inactivated whole serum, however, can hardly be regarded as a satisfactory or indeed as an acceptable "vaccine".

An immunochemical study of the purified antigen is essential for the understanding of this unique antigen. Analogous to the tobacco mosaic virus coat protein decapeptide the primary sequence of the haptenic peptide of hepatitis B antigen may provide a basis for a development of a synthetic peptide which, when coupled to human albumin, could serve as a suitable immunogen. In last Wednesday's issue of *Nature New Biology* (**241**, 240; 1973) K. R. Rao and G. N. Vyas describe the preparation of active subunits of hepatitis B antigen by sonication and chromatography. This may provide a lead for the preparation of a "synthetic" material containing the immunogenic determinant. Isolated viral coat protein challenges the body's immune mechanism in the same way as the whole infectious agent. It is widely believed now that hepatitis B antigen (Australia antigen) represents incomplete viral particles in the form of aggregates of protein subunits or excess viral coat protein.

Once detailed data are available on the protein, peptide and amino-acid composition of hepatitis B antigen, it should be possible to define by animal immunization the moiety responsible for the antigenic activity. Infectivity studies can be carried out in appropriately selected subhuman primates such as rhesus monkeys and, in due course, possibly also in culture preparations of liver.

There are reports in the literature to support the feasibility of such an approach. For example, in 1966 J. M. Stewart and colleagues (*Biochemistry*, **5**, 3396; 1966) defined the antigenic moiety of TMV protein decapeptide. R. Arnon and her colleagues (*Proc. US Nat. Acad. Sci.*, **68**, 1450; 1971) showed that it was possible to use a synthetic macromolecule for eliciting antibodies reacting exclusively with a specific region of a native egg-white lysozyme. This was achieved by synthesizing a particular segment of the enzyme from its amino-acid components, attaching the peptide to a synthetic polypeptide carrier and using the conjugate for immunization. The resulting antibodies reacted with native lysozyme in a unique, conformation-dependent antigenic determinant. Of course, in the case of lysozyme both the amino-acid sequence and the three-dimensional structure are known, and the synthesized peptide was designed on the basis of previous information concerning its contribution to the antigenic specificity of the molecule.

A similar approach might be attempted for type B hepatitis, depending largely on the success in elucidating the structure of hepatitis B antigen. There is little doubt that polypeptides and other moieties such as specific lipoproteins can be attached to a macromolecular carrier (M. Sela, *Adv. Immunol.*, **5**, 29; 1966) for subsequent immunization. Speculative? Perhaps, but an exciting challenge nonetheless.

From our Medical Virology Correspondent.

Caps and Patches on Lymphocytes

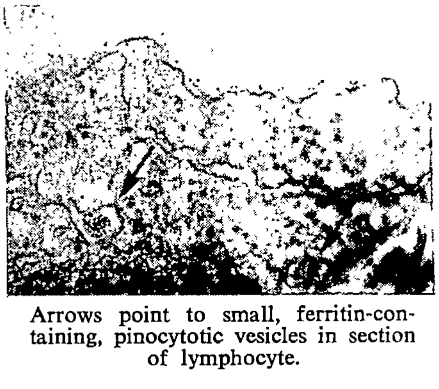
OPTIMISM is a sterling attribute for the biological scientist who would otherwise readily become bewildered by the complexities of the materials under study. Lymphocytes are thought of and manipulated by many contemporary cellular immunologists who tend to think of them as units of function in immune responses. But it has been apparent for some time that the interaction between a lymphocyte and the antigens to which it responds is susceptible of investigation at the boundary of the cell with its environment—the plasma membrane.

It has been shown (Taylor *et al.*, *Nature New Biology*, **233**, 225; 1971) that attachment of cross-linking antibodies to the immunoglobulins which are found on the surfaces of some lymphocytes can cause migration of the bound molecules to one pole of the cell and the formation there of a "cap". This process of capping *in vitro* requires metabolic activity by the cell and could not be induced by using monovalent antisera. In an article in next week's *Nature New Biology* (February 28) de Petris and Raff carry these investigations further.

In the earlier report Taylor *et al.* used fluorescent anti-immunoglobulins to cause capping and as a visual indicator of the process. In the new studies de Petris and Raff used ferritin-bound antibodies followed by electron microscopic examination by which the ferritin molecules can be visualized and their locations used as a manifestation of the process of capping (see figure). Their new conclusions bear out the results of the earlier studies and make two important additional observations. First, they find that when divalent cross-linking ferritin-bound antibodies are used to cause cap formation there is a prior formation on the cell surface of patches, which represent dense aggregates of antibody bound to the immunoglobulin target molecules. These patches are not observed when monovalent antisera are used and they do not therefore represent the distribution of immunoglobulins in the unperturbed membrane but are a consequence of cross-linking. Interestingly, and unlike capping, patch formation can occur in the presence of metabolic inhibitors such as sodium azide and at low temperatures.

Second, de Petris and Raff find that pinocytosis can occur on a small scale and after some time without cap formation when a monovalent antiserum has been used. They therefore conclude that cap formation and pinocytosis are independent phenomena.

These are interesting studies but it should be emphasized that an *in vivo* equivalent to cap or patch formation is not yet known. Neither is it yet obvious what role either process has in relation to the performance of the affected cell in an immune response. On the optimistic hypothesis that because these processes exist they must have biological significance, the further development of this work should be of great interest.



Arrows point to small, ferritin-containing, pinocytotic vesicles in section of lymphocyte.

TUMOUR BIOLOGY

Chemical Transformants

from our Cell Biology Correspondent

THE properties of chick embryo fibroblasts infected and transformed by certain temperature sensitive mutants of Rous sarcoma viruses have established that the maintenance of the transformed cell phenotype depends upon the continuous expression of one or more viral functions. Similar experiments with a solitary temperature sensitive mutant of polyoma virus lead to the same conclusion. Both the RNA and the DNA tumour viruses have small genomes and it seems unlikely, to say the least, that each and every change in the phenotype of the cell transformed by one of these viruses results directly from the action of a distinct viral protein. The viruses simply do not have enough genetic information to be so profligate. It follows therefore that the limited number of transforming proteins specified by the tumour viruses must induce either pleiotropic effects or they must interact with various cellular molecules and indirectly bring about transformation.

At present the nature of the transforming viral proteins is not known, neither is anything known about the putative cellular molecules which may be targets for the viral proteins. But just as it is possible to inactivate by mutation the viral genes involved in transformation, it ought to be possible to mutate the cellular genes specifying the target molecules, and Di Mayorca *et al.* (*Proc. US Nat. Acad. Sci.*, **70**, 46; 1973) may have done this; certainly the data they present can be so interpreted.

Di Mayorca *et al.* exposed BHK$_{21}$ clone 13 cells to dimethylnitrosoamine or nitrosomethylurea and then plated the cells in liquid media to measure their plating efficiency and in soft agar to measure their ability to grow in suspension into colonies. These BHK cells do not grow in agar suspension unless they have been transformed and this technique of suspension plating has been widely used as a method of selecting and assaying for transformation of BHK cells. Using these procedures Di Mayorca *et al.* detected transformants at a frequency of 6×10^{-6} in populations of BHK cells exposed to appropriate doses of either dimethylnitrosamine or nitrosomethylurea. That transformants arise after exposure to these chemical carcinogens/mutagens is not in itself particularly surprising, but the phenotype of the transformed cells is remarkable. Apparently all the transformants isolated after the cells have been exposed to the carcinogens as well as a single clone of spontaneously transformed BHK cells prove to be temperature sensitive for the two markers of the transformed state that were assayed—the ability to grow in agar suspension and the morphology of the colonies. In all cases these transformants failed to grow in agar at 32° C and in liquid media grew to form typical monolayers, but at 38.5° C they behaved as transformed cells growing to form colonies in agar and to form multilayered foci in liquid medium.

These results are apparently fully reproducible and the properties of these chemical transformants are in marked contrast to the properties of BHK cells transformed by polyoma virus which exhibit the transformed phenotype at 32° C and 38.5° C. These temperature sensitive chemical transformants also differ from cells transformed by temperature sensitive tumour viruses, the latter having a transformed phenotype at lower temperatures and an untransformed phenotype at higher temperatures.

The obvious interpretation of these data which Di Mayorca *et al.* offer is that the cells they have isolated carry a temperature sensitive lesion in a cell gene which specifies a product required for the maintenance of the normal or untransformed phenotype. They suggest that at 32° C the putative cellular gene product is functional whereas at 38.5° C it is inactivated because of a temperature sensitive mutation and as a result the cells acquire the transformed phenotype as their temperature is raised. Clearly if such a cellular gene product, that is required to maintain a cell in the untransformed state, exists it must be inactivated when a cell is transformed by a tumour virus; it must presumably be inactivated, for example, when BHK cells are transformed by polyoma virus and this putative cellular protein may be a target of the viral transforming gene proteins.

No doubt such speculations are not to everybody's taste, but surely few would deny that the cells which Di Mayorca and his colleagues have isolated have remarkable properties.

TEMPERATE VIRUSES

Infection in Humans

from our Medical Virology Correspondent

SUBACUTE sclerosing panencephalitis (SSPE), a fatal disease of children and young adults, is a chronic progressive infection of the central nervous system by a measles-like virus (M. Katz *et al.*, *Nature*, **222**, 888; 1969; and V. Ter Meulen *et al.*, *Curr. Topics Microbiol. Immunol.*, **57**, 1; 1972). The evolution of the disease can be divided into clinical stages characterized by mental and behavioural changes, disorders of the locomotor system and loss of cerebral-cortex function. The SSPE agent has many of the biological properties of measles virus, but unlike conventional strains of measles it remains intimately bound to cells and it has a different pattern of replication and intracellular behaviour.

The chronic nature of this viral infection, the possibility that the formation of immune complexes may be important in the aetiology of this disease and perhaps in causing some of its damage to nervous tissue (A. D. Dayan and M. I. Stokes, *Brit. Med. J.*, **2**, 374; 1972) suggest that SSPE may be a model of temperate viral infections in humans, possibly an important group

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Transformation by Herpesvirus

SOME herpesviruses of mammals are known to possess an oncogenic potential, and Duff and Rapp (*Nature New Biology*, **233**, 48; 1971) believe that herpes simplex virus, a human virus, can transform hamster cells. Whether herpes simplex virus or any of the other herpesviruses which are indigenous to man have any role in the development of cancer in human beings is, however, another and a vexed question. Obviously human herpesviruses, which can be shown to transform human cells in culture, must be seriously considered as potential human carcinogens and for this reason numerous groups are carrying out the appropriate experiments. Darai and Munk in Heidelberg, for example, have been investigating the infection of human embryonic lung cells with *Herpesvirus hominis* type 2, and they report in next Wednesday's *Nature New Biology* (February 28) that when cultured in appropriate conditions the infected cells have some of the properties characteristic of transformed cells.

The complete replication of *Herpesvirus hominis* in cultures of human lung cells results in cell lysis, and to prevent this Darai and Munk raised the temperature of the culture 1 hour after infection from 37° to 42° C. Cells which survived infection for eight days at 42° C were then returned to 37° C and repeatedly subcultured. Several cell lines were established and these cells were tested in a variety of ways.

The cells all proved to contain a *Herpesvirus hominis* antigen in the cytoplasm; to tend to form syncytia as a result of cell fusion apparently promoted by a viral-coded cell surface like a protein; to resist superinfection and to survive longer in culture than control uninfected cells. These properties suggest that the cells may have been transformed.

of disorders in man including such divergent diseases as viral hepatitis (A. J. Zuckerman, *Immunopathology* VI, edit. by P. A. Meischer, Schwabe, Basel, 1971, p. 436) and multiple sclerosis (F. Wolfgram *et al., Multiple Sclerosis, Immunology, Virology and Ultrastructure,* Academic Press, 1972). This is now the subject of intensive investigation in many laboratories.

Traditionally the tissue damage caused by viral infections has been explained by the ability of viruses to multiply in cells, thereby leading to cell injury or destruction. It is now becoming clear, however, that other mechanisms may be operating and that lesions may be caused by the immune response of the host to viral antigens and that the immune system itself may be disturbed by some viruses. Thus, certain viruses depress the humoral and cellular immune responses of the host, whereas other viruses may enhance the antibody response. Several viral antigens persist in the circulation and combine with specific antibody resulting in antigen-antibody complexes. These complexes may lodge in various sites, and in other instances combination with complement releases substances which cause tissue damage. Immunological injury mediated by antibodies may also result when new antigens produced by viruses on infected cell surfaces interact with specific antiviral antibody and complement (Memorandum: Virus-associated Immunopathology, *Bull. Wld Hlth Org.*, **47**, 25 ; 1972).

This concept of virus-associated immunopathology has recently been extended to temperate viral infections and it is possible that the ability to produce infectious immune complexes may be important in establishing chronic infections such as SSPE and hepatitis B in man and lymphocytic choriomeningitis, aleutian mink disease and murine sarcoma and leukaemia in animals. Chronicity may be attributable to differences in the affinity of the antibodies produced, a factor which is partly under genetic control, perhaps on mechanisms linked to histocompatibility genes (W. F. Bodmer, *Nature,* **237**, 139 ; 1972). It is difficult, however, to explain the relative rarity of SSPE, if it is caused by measles virus, in the face of the ubiquitous distribution of measles. What is needed is an animal model, but experimental inoculations of animals with different strains of SSPE agent have generally yielded divergent results. P. Albrecht and colleagues (*J. Infect. Dis.*, **126**, 154 ; 1972) have reported recently that a hamster-brain-adapted strain of measles virus produced encephalitis in rhesus monkeys with morphological findings similar to those described in SSPE and quite unlike acute measles encephalitis in man. The principal property responsible for this potential of measles virus seems to be an aberrant intracellular replicative cycle of the virus which affects the maturation process at the cell membrane. Further understanding of temperate viral infections in humans thus seems likely in the near future.

PHOTOPHOSPHORYLATION

Without Membranes

from our Photosynthesis Correspondent

IN 1954 it was discovered that isolated chloroplasts could utilize light energy to make adenosine triphosphate (D. Arnon *et al., Nature,* **174**, 394). This finding had important implications because it meant that chloroplasts could produce ATP as well as $NADPH_2$ for driving CO_2 fixation. Photophosphorylation is now a well documented phenomenon which can readily be detected with lamellae fragments obtained from chloroplasts which have been broken osmotically. It has even been shown to occur in small subchloroplast vesicles obtained either by sonication (R. E. McCarty, *J. Biol. Chem.*, **244**, 4292 ; 1969) or by treatment of inner lamellae with digitonin (N. Nelson *et al., ibid.*, **245**, 143 ; 1970). The common feature of these phosphorylating systems was that they were dependent on the presence of an intact membrane and also they required the addition of electron carriers or acceptors. It now seems possible, however, that photophosphorylation can occur in the absence of both intact membranes and artificially supplied electron carriers.

McPhee and Brody (*Proc. US Nat. Acad. Sci.*, **70**, 50 ; 1973) report the striking observation that an acetone extract obtained from chloroplasts when layered on an aqueous surface will exhibit light-induced phosphorylation. The extract was obtained from particles derived by sonicating spinach chloroplasts, and was used to produce a monolayer at an air-water interface by compression to a surface tension of about 20 dynes cm^{-1}. Electron microscopy indicated the films to be partly composed of small structured particles of about 200 Å diameter at a concentration of one particle per 2×10^8 $Å^2$ of compressed surface. On illumination McPhee and Brody detected ATP production with quantum yields between 0.1 and 1. The ability of the monolayer to catalyse photophosphorylation was dependent on maintaining a compression of at least 10 dynes cm^{-1} and could be doubled by adding phenazine methosulphate.

The artificial system was also found to induce additional esterification of inorganic phosphate not directly correlated with ATP formation. To explain their results McPhee and Brody argue that the phosphorylation observed may take place by a two-step reaction, one involving transphorylation between two ADP molecules to yield AMP and ATP followed by esterification of AMP to ADP.

Although McPhee and Brody have not used their data to discuss the chemical (E. C. Slayter, *Eur. J. Biochem.*, **1**, 31 ; 1967) or chemiosmotic (P. Mitchell, *Biol. Rev.*, **41**, 445 ; 1966) hypotheses their observations will undoubtedly be used by the "anti-chemiosmotic school" in attempts to dislodge Mitchell's elegant hypothesis.

Poly(A) Tract and Messenger RNA Ageing

THE function of the tracts of adenylic acid residues that are known to occur at the 3′ ends of many messenger RNA molecules remains a mystery, but experiments reported by Sheiness and Darnell in *Nature New Biology* next Wednesday (February 28) indicate that as messengers age in the cytoplasm of HeLa cells the length of the poly(A) tracts decreases ; this may be a clue to their function.

Sheiness and Darnell analysed the poly(A) liberated by ribonuclease from populations of messenger RNAs in cytoplasmic extracts of HeLa cells fed pulses of ^3H-adenosine and then actinomycin D. They conclude from such experiments, first, that the tracts of poly(A) in cytoplasmic messengers shorten as a result of metabolic ageing and, second, that this shortening occurs in the cytoplasm after the messengers have been transported from the nucleus. Furthermore, this time-dependent shortening of the poly(A) tracts occurs when protein synthesis is blocked. It seems plausible to suggest therefore that the lifetime of a messenger may be determined by the length of the 3′ poly(A) tract and the rate at which the messenger loses adenylic acid residues. In other words, the function of poly(A) tracts of messengers may be to programme the lifetime of the molecules.

Also in *Nature New Biology* next week Gross *et al.* report the isolation from the polysomes of sea urchin embryos of a "9S" RNA fraction which stimulates a cell-free system from Krebs II mouse ascites cells to incorporate amino-acid. Fingerprint analysis of the product of *in vitro* translation indicates that it includes histones, and by comparing the stimulation of incorporation of tyrosine and tryptophan by 9S RNA Gross *et al.* conclude that their 9S RNA seems to be relatively free of contamination by messengers for proteins other than histones.

NUCLEIC ACIDS

Conformation Contorted

from our Molecular Biology Correspondent

GONE are the days when DNA was seen as nothing more than a repository of information, which did nothing but sit in the chromosome waiting to be transcribed. It is still by no means clear that the canonical structural forms, other than the B structure, which is presumed to be that of native DNA in aqueous media, have any functional significance, although the rather ill-founded notion is gaining ground that DNA in the chromosome is partly in the C form. What does seem clear is that the potential for conformational change in response to environmental disturbances is built into the molecule, and with it a rich harvest of speculation, ripe for the gathering.

The dearth of hard information, especially in regard to the state of DNA when associated with basic molecules, is such that a study by Suwalsky and Traub (*Biopolymers*, **11**, 2223; 1972) on the X-ray diffraction of such complexes comes as an agreeable change. They have examined nucleoprotamine from sperm heads, and also complexes with polylysine and polyarginine as a function of humidity. The principal upshot is that, at least at high humidity (and therefore by implication in solution), the DNA is in all cases in the B form. The structures have not been explicitly solved, and probably complicated by intermolecular interaction modes. It seems clear, however, that in both nucleoprotamine and the polysine complex the polypeptide chain is strung along the narrow groove of the double helix. In spite of the high arginine content of protamines, the polyarginine seems to bind in a different manner. At low humidity, the DNA in the polysine complex goes into the C form, but in the presence of polyarginine this transition does not take place. The results should perhaps help to discourage some of the more uninhibited interpretations of the very striking optical properties of such complexes, which tend to invoke unusual DNA conformations.

Interesting optical effects also occur in complexes of DNA with large amounts of histones, which have been systematically explored by Fasman and his associates and by others. More data on the circular dichroism of complexes with F1 histone have now been collected by Šponar and Frič (*ibid.*, 2317). The circular dichroism in these systems is changed in shape and grossly intensified, and Šponar and Frič find that whatever interaction causes this phenomenon is a function of base composition, the largest effects occurring with DNA of high GC content. The curves rather resemble those of Lerman's ψ-form, which is characteristic of DNA in solutions containing salts and neutral non-interacting polymers. Interpretation in such situations tends to run far ahead of the data. That it is all fraught with meaning may, however, be apparent from the results of Adler, Langan and Fasman (*Arch. Biochem.*, **153**, 769; 1972), who have found a remarkable effect on the circular dichroism of the complexes with F1 histone of phosphorylation. This occurs enzymatically at two serines, and the result is that the effect of the histone on the circular dichroism is substantially eliminated. Phosphorylation of either serine gives about half the effect. Merely introducing a few new negative charges, as by chemical maleylation, has no such influence on the optical activity. Sedimentation experiments indicate that the phosphorylation does not noticeably affect the affinity of the DNA for the histone, which is very basic. It therefore seems as though some structural feature of the interaction of F1 is altered by phosphorylation, which occurs physiologically at the two sites.

It may come as no surprise that the miasma of allosterism is now beginning to engulf DNA. Pohl *et al.* (*Proc. US Nat. Acad. Sci.*, **69**, 3805; 1972) have come up with an interesting system, in which a structural change in DNA is indeed triggered by a ligand, and because of the high conformational cooperativity associated with long DNA helices the effect is rather dramatic. Like other DNAs, the alternating polymer, poly (dG.dC), evidently undergoes some form of structural change in solutions of high ionic strength, which is characterized by an inversion of Cotton effects in the ultraviolet circular dichroism. This is a slow first-order intramolecular process. Now the dye, ethidium bromide, binds to DNA by intercalation between the base pairs, in this particular DNA to the extent of one dye to two base pairs at saturation. What Pohl *et al.* have now found is that at high salt concentration the binding to a polynucleotide of high molecular weight becomes acutely co-operative, and goes from zero to full saturation within an almost imperceptibly narrow range of dye concentration. This is most felicitously explained in terms of what is indeed a kind of allosteric effect, whereby the low-salt form of the DNA has a very high, and the high-salt form a very low, affinity for the dye. At a critical dye concentration the conformation is therefore sucked abruptly into the low-salt form.

Circular dichroism of the dye complex at high and low ionic strength confirms that the conformations are similar. The kinetics, monitored by the fluorescence change of the ethidium on binding, are consistent with the demands of such a scheme. The value of the "allosteric constant", the equilibrium constant relating the low and high-salt forms in the absence of dye, which best fits the data, agrees with the value obtained by earlier work on the salt-induced transition of the polymer. Whether such finely poised transitions of DNA occur in life is, of course, at this stage anybody's guess.

A quite different type of conformational problem is the prediction of RNA structures when there is only partial internal complementarity. Im-

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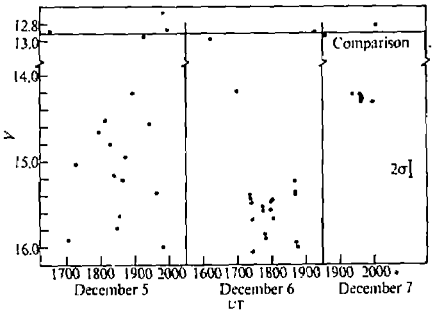
Rapid and Strong Variations in BL Lac

IN next Monday's *Nature Physical Science* (February 26) Weistrop reports observations of the unusual object BL Lac carried out at the Florence and George S. Wise Observatory in Israel. BL Lac is intriguing because it exhibits many of the properties of QSOs but has no lines in its visible spectrum. It has been speculated that this object, and two or three similar objects, might be blueshifted QSOs.



Variability of BL Lac (lower part) compared with a standard reference star observed by the same telescope on the same nights.

Weistrop's observations were made on three nights in December 1972. They show evidence of extremely strong short-term variability in the source (see diagram) during periods much less than 1 h on December 5, 6 and 7. Previously, other observers have noted changes in the brightness of BL Lac of a few tenths of a magnitude in one night and by as much as 1.3 mag within 20 h. The present data indicate changes of 1.5 mag within 1 h, and there is a hint of repeated patterns occurring over 85 min. On at least two occasions, says Weistrop, variations of 0.5 mag occurred within a few minutes. All this evidence points to the occurrence of extremely violent processes in BL Lac, making the object even more of a prime target for further observations.

portant steps in this direction are revealed in two articles, which treat of the stability of short helices, joined by loops of unpaired bases. In a molecule such as $A_nC_mU_n$, the existence of a flexible link of C residues will favour the pairing of the A with the U, when m is not too large or too small. Uhlenbeck *et al.* (*J. Mol. Biol.*, **73**, 483; 1973) have made a series of such molecules with $n=6$ and m varying between 4 and 8. When the loop is only four or five residues long, it is evidently strained, and the probability of A–U pairing is less than theoretically expected; indeed circular dichroism gives evidence of an unusual geometry for the single-stranded cytosine residues when $m=5$. The most favourable situation occurs at $m=6$. Gralla and Crothers (*ibid.*, 497), working with the oligomer series $A_4GC_nU_4$, arrive at similar conclusions. If $n=4$, the loop is too tight and, in spite of the entropy loss, intermolecular interaction is preferred, because to make an easier intramolecular loop, the G–C pair would have to be prised open. In the range n from 4 to 6, the intramolecular fold thus becomes more stable with increasing loop size. The thermodynamics and statistical mechanics of these systems are treated in both articles in a manner to which one cannot do justice without a fuller account. Some interesting implications regarding tRNA conformation can be drawn.

STEROIDS

Testicular Oestrogens

from a Correspondent

IT has long been recognized that males and females secrete the same type of steroid hormones and the difference between the sexes is quantitative, the ovary producing predominantly oestrogens and the testis producing predominantly androgens, in particular testosterone. Many of the hormones, in addition to direct secretion from the gland, may arise by the peripheral conversion of precursors.

A large amount of circumstantial evidence suggests that in man the testis secretes oestrogens: oestrogenic material can be found in extracts of testes and testicular tissue incubated *in vitro* can convert suitable precursors to oestrogens. Application of constant infusion techniques and measurement of the steroids both in blood and urine, however, has produced conflicting evidence; some results suggest that about half of the circulating oestrogens in the male are secreted by the testis, the remainder arising from circulating precursors, whereas other experiments suggest that there is no direct secretion from the testis. There is now direct evidence to support the former view.

In one study (Longcope *et al.*, *Steroids*, **20**, 439; 1972) young males, who were undergoing renal vein catheterization as part of an investigation of essential hypertension, had samples of blood removed by catheterization from the inferior vena cava below the entrance of the spermatic vein and a second sample was taken from the spermatic vein itself. The concentrations of testosterone, oestradiol and in some cases oestrone were higher in the spermatic vein samples than in the samples from the inferior vena cava. These findings confirm the report of Kelch *et al.* (*J. Clin. Invest.*, **51**, 824; 1972) of a positive gradient for oestradiol across the testis in anaesthetized humans. The testis, like the ovary, seems to secrete more of the 17β-hyroxysteroid (oestradiol) than the 17-oxosteroid (oestrone) in contrast to the adrenal cortex which secretes predominantly the 17-oxosteroid. The cellular origin of testicular oestrogen and particularly its function remain to be determined.

VISION

A New Slant

from our Experimental Psychology Correspondent

THE discoveries by Hubel and Wiesel of neurones in the visual system, each specifically sensitive to a line segment or edge in a particular orientation, have been regarded as of great significance and importance. Yet in spite of widespread interest, and in spite of the fact that these discoveries are now fourteen years old, there is still little clue as to the role of these cells in perception. Hirsch and Spinelli (*Science*, **168**, 869; 1970) and Blakemore and Cooper (*Nature*, **288**, 477; 1970) seemed to hold out some hope for insights into function by showing that in cats reared in environments where they saw only horizonal or vertical lines, neurones in the visual cortex responded only to stimuli at or near the orientation to which they had been exposed. And indeed this effect of early environment on responsiveness of cortical neurones seems relatively clear. But now Hirsch (*Exper. Brain. Res.*, **15**, 405; 1972) has reported on the behavioural experiments which form the complement of this research, and these indicate that the effect of the physiological changes on perception still defies adequate explanation. Hirsch's experiments were on some of the cats in his orientation-specific rearing series which had had electrophysiological recordings made from their visual cortices. When they had recovered from this procedure Hirsch ran them in some discrimination tasks.

The experiments are a little unsatisfactory in that only six of the cats reared with horizontal and vertical visual environments were tested, and in some tests only two of these animals took part. Thus what differences there were between the groups and between the experimental animals and normal controls cannot be regarded as very reliable. It is the finding that cats could perform visual tasks involving shape and orientation discrimination at all with such substantial reduction of their orientation-sensitive neuronal apparatus that is striking.

These cats were raised with all their visual experience in the light confined

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Differences between Red Sea Brine Pools

OCEANOGRAPHER DEEP, which is the most northerly of the brine pools in the Red Sea, was discovered in 1967 by echo sounding from the research vessel Oceanographer. In next Monday's *Nature Physical Science* (February 26) Tooms and his colleagues of Imperial College, London, report the analysis of a sediment core recovered during a cruise of the tug Nereus in 1971. The bottom of Oceanographer Deep is about 570 m below the seafloor on either side, and is outside the median valley of the Red Sea. It is about 2 to 3 nautical miles long and 0.6 nautical miles wide about 200 m from the bottom.

Analysis of the core and the water in the core liner above the sediment revealed that although the water is a concentrated brine—the chlorinity of 16 per cent is quite similar to that of Atlantis II Deep—the amounts of trace metals such as iron and copper are very low by comparison with brines from other deeps in the Red Sea. For example the 56° C brine from Atlantis II Deep contains 0.08 g kg^{-1} iron by comparison with 0.2 mg kg^{-1} for Oceanographer Deep and 0.02 mg kg^{-1} for normal seawater.

Tooms *et al.* say that the core itself has concentrations of metallic elements comparable with those reported for anoxic Norwegian fjords. The smell of H_2S associated with the core and the fact that there was considerable shrinkage during storage indicate that the original environment of the core was strongly reducing.

One of the possible explanations of the brine in Oceanographer Deep suggested by Tooms *et al.* is that it arises from the dissolution of evaporite deposits in surrounding seawater rather than from tectonic activity. They go on to suggest that similar brines might be present in depressions in the seabed of, for example, the Mediterranean Sea where evaporite deposits are known to occur.

by wearing translucent goggles, so that one eye saw only a field of horizontal stripes and the other only a field of vertical stripes. In the electrophysiological experiments the orientation-sensitive neurones that were found responded to the orientation of rearing for the eye being tested and these cells could typically not be affected by stimuli shown to the other eye. Nevertheless, behaviourally Hirsch found that in these animals discrimination of shapes and orientations trained entirely with one eye could be performed (though somewhat less well) when tested on the other.

The findings of Hirsch with discrimination of orientations around vertical and around horizontal are perhaps the clearest. Here cats tested with the eye reared on vertical stripes performed better than with the eye reared with horizontal stripes in the discrimination of orientations around vertical. Similarly when using the eyes reared with horizontal stripes and tested around horizontal they were better than when using those reared with vertical. And cats reared normally did a little better still.

The important finding, however, was that differences between the groups were rather small and cats did manage to perform discriminations between those orientations for which they evidently lacked cortical neurones. Further electrophysiological study of these same cats following the behavioural experiments confirmed that the deficit of neurones sensitive to orientations other than those with which they were raised still existed.

One might have supposed that orientation-sensitive neurones would at least be used in making discriminations between lines of different orientation, but perhaps even this must be rethought. One cannot, on the basis of these experiments, immediately dismiss the idea of neurones in the visual cortex as feature detectors, but once again the brain seems to be more subtle and versatile than one would have given it credit for.

POPULATION ECOLOGY

Fighting a Forest Pest

from our Soviet Correspondent

A NEW mathematical theory of insect population dynamics may facilitate the preservation of forests from xylophagic insects without the excessive use of insecticides, which may themselves be harmful to standing timber. This approach, developed by A. S. Isaev, of the Sukachev Forestry Institute, and R. G. Khlebopros, of the Siberian Branch of the Soviet Academy of Sciences (*Dokl. Akad. Nauk SSSR*, **208**, 225 ; 1973), is based on the concept of a "critical" population density at which ecological balance breaks down and the establishment of the "multiplication factor"—the ratio of insect density in the $(n+1)$th generation to that in the nth.

Isaev and Khlebopros estimated the multiplication factor as a function of population density itself, the quantity and type of food, various external factors independent of the population density and the lag in the natural regulatory processes of forest ecology. They found that, for a constant type of food, a stability level should be established, around which population density should fluctuate in a manner dependent on the availability of that food. But as certain types of insect, notably the horned beetle *Monochamus urussovi*, increase in population density, regulation of the population by overconsumption of their food does not occur ; above a certain "critical" density, the feeding habits of such insects become modified to include a great range of plants. When this "critical" density is exceeded, the possibility of a second stability level of population in equilibrium with food supplies does, of course, exist ; in practice, however, this will not occur until there has been a massive disruption of the ecology and widespread devastation of the forest, such as *Monochamus urussovi* has produced in recent years in the fir forests of Central Siberia.

To remedy this situation, in localities where the local population density of insects has increased above the critical level, Isaev and Khlebopros suggest the use not of insecticides but of insect repellents which, without harming the trees, would disperse the insects into surrounding areas and thus reduce the population density below the critical level. This would create a situation in which the natural regulating factors of forest ecology would gradually reduce the density of the population.

OCEANOGRAPHY

Polygons and Waves

from a Correspondent

LONGUET-HIGGINS, of the University of Cambridge, has discovered a new and remarkably simple approximation for the profile of the steepest possible gravity waves which can occur in deep water (*Proc. Roy. Soc. Lond.*, **A331**, 445 ; 1973). The usual conditions for a gravity wave are that the fluid be inviscid, incompressible and irrotational, that surface particles move with the surface, and that the pressure be constant over the surface. Expressed mathematically, these conditions give rise to non-linear equations which, strictly speaking, have never been completely solved.

The simplest approximation is to assume that the slope of the surface is everywhere very small (say less than 1 in 10). One may then ignore the nonlinearities, and obtain the well-known

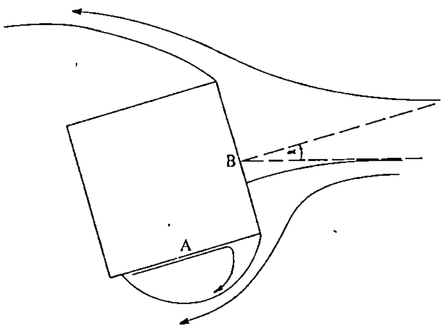
More about Aerodynamics of Buildings

ONE of the more important things that have to be taken into account when designing a building is how the structure will behave in a wind. To this end many people have in the past examined what happens when cylinders of square cross-section, typifying many buildings or their component parts, are exposed to rapid air flow in a wind tunnel.

In *Nature Physical Science* next Monday (February 26) Mulhearn describes such an experiment which he carried out in the 4 foot by 5.5 foot closed-circuit wind tunnel in the Engineering Laboratories at the University of Cambridge. He used a cylinder with 6-inch sides which was exposed to a wind of velocity 70 foot s^{-1} (about 50 mile h^{-1}).

Earlier investigators, such as Vickery, established that the resistance of a square cylinder to wind decreases when the flow becomes turbulent. Vickery contended that turbulence promotes reattachment of the flow, which originally separated from the leading face of the cylinder (see diagram), at a position closer to the leading edge than is the case for non-turbulent flow. Bearman and Kavur, however, found that no reattachment occurred in cases where the angle of incidence α was small.

Mulhearn's observations neatly suggest a compromise, in that he finds no reattachment at small angles of incidence but that the phenomenon does occur at larger values. He has confirmed the earlier finding that reattachment occurs sooner when the flow is turbulent, and he says that this implies that, even when reattachment does not occur, the shear layers emanating from the leading corner are closer to face A.



What is still not clear, however, is why resistance should be decreased as the separated shear layer comes nearer to the surface.

linear wave solutions with sinusoidal profiles and dispersive properties. Going one step further, the non-linear terms may be partially restored by substituting the first approximation to obtain the "Stokes wave" (Lamb, *Hydrodynamics*, art. 250, Cambridge University Press, 1932), which has flatter troughs, and crests of greater curvature, than the sinusoid. This tendency increases as the steepness is allowed to increase until ultimately, Stokes showed, a limiting form for the progressive wave should be obtained, which has a sharp symmetrical wedge-shaped crest enclosing a perfect angle of 120° (maximum slope 30° from the horizontal). Unfortunately, the method of trying to approach the 120° crest by a series of approximations from a sinusoid fails to converge.

Stokes worked in the second half of the nineteenth century; since then a succession of mathematicians have attempted by various means to formulate the full profile of the 120° wave. Basically they all give slightly different results (for the ratio of height to wavelength, for example), and nearly all involve numerical computations which are strenuous even by modern standards. The standing wave presents similar problems and, by contrast, is limited by a 90° crest. It is interesting to observe that although the limiting standing wave has a peak vertical acceleration of $-g$, so that particles at the crest are momentarily "weightless", the corresponding acceleration for the limiting progressive wave nowhere exceeds $-\frac{1}{2}g$.

Longuet-Higgins has derived his formula by the elegant trick of conformally transforming a regular polygon. A hexagon transforms into a wave-like profile with perfect 120° crests; a square yields 90° crests, corresponding to the limiting standing wave. All the hydrodynamical conditions are satisfied except that of constant pressure, but the actual pressure distribution is shown to be within 7 per cent of uniformity. And the profile is so close to the results of laborious numerical approaches as to be nearly indistinguishable on an ordinary graphical plot. Its greatest virtue is its simplicity. With suitable scaling the profile may be written

$$y = \ln \sec x$$

with trough at $x=0$ and crests at $x = \pm\pi/6$ (progressive wave) or $\pm\pi/4$ (standing wave). Simple formulations also exist for the fields of velocity and acceleration. These properties will appeal to marine engineers, who are notoriously sceptical of abstruse mathematical formulae but very concerned with the properties of the steepest waves which are precisely those responsible for the wrecked oil rig or the capsized trawler.

MATERIALS

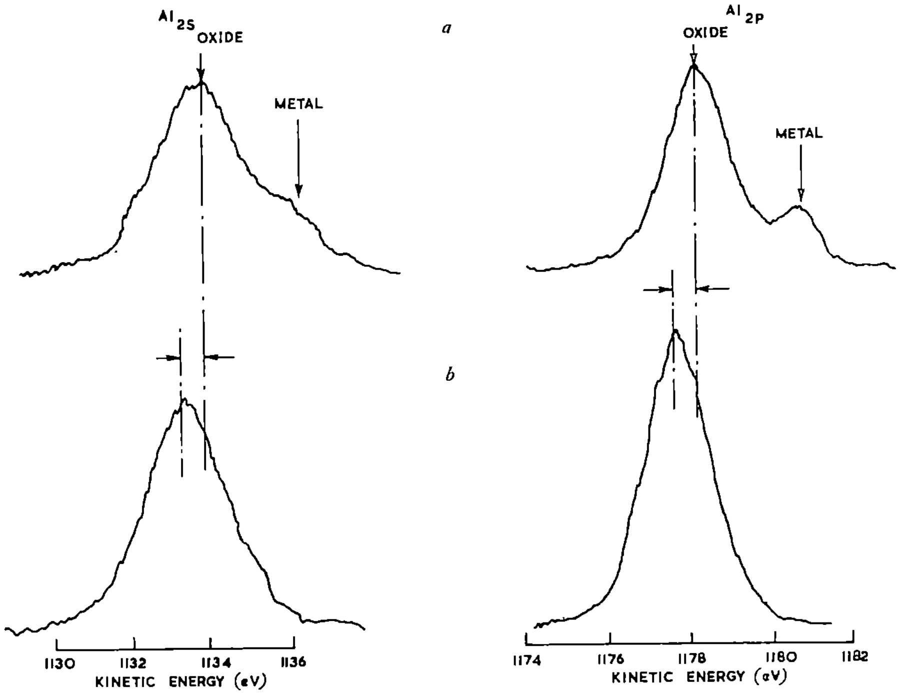
Anomalies in Perspex

In the latest of a series of reports about undergraduate projects which have produced worthwhile results, Puttick, of the University of Surrey, describes some curious features of Perspex in *Journal of Physics E: Scientific Instruments* (**6**, 116; 1973). Much of the experimental work was carried out by Jewers, then a third-year undergraduate at the University of Surrey, under supervision.

The experiment involved a study of how Perspex indents and fractures when a steel ball bearing (3.2 mm) is driven into the surface at speeds of, typically, between 0.017 and 1.7 mm s^{-1}. The work revealed some interesting features of the way in which cracks develop under these circumstances, but it also brought to light a strange phenomenon that was observed to particular advantage when specimens were unloaded before fracture could occur.

An example is shown in the figure; a spherical region of anomalous refractive index is generated beneath the indentation, and this region defines the inner boundary of the crack, which Puttick likens to a sycamore seed. By applying elementary optics to what amounts to a thick lens embedded in a medium, it turns out that the difference in refractive index is $+1.7\times10^{-3}$ and that the change in density in the spherical region, $\delta\rho/\rho$, is 2.9×10^{-2}. By comparison, assuming that all the material that was in the crater (apart

ESCA Probes the Oxide Films on Aluminium

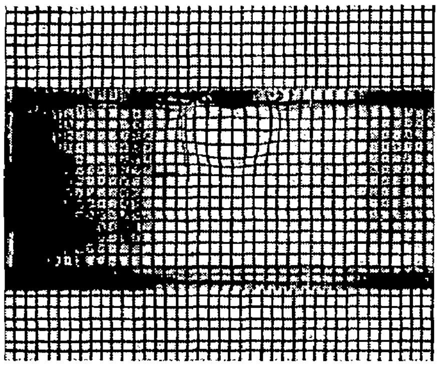


a, Hot-rolled aluminium sheet; *b*, similar sheet heated in an oxygen-rich flame.

According to the literature on the subject, the most recent of which is dated 1954, the thickness of the oxide film (γAl_2O_3) on aluminium manufactured at temperatures above 400° C can be as large as 2,000 Å. Why then does aluminium produced in this way have a shiny appearance? In next Monday's *Nature Physical Science* (February 26) Tripathi and Clark describe measurements made by ESCA (electron spectroscopy for chemical analysis) which show that the thickness of the film is in fact about 15 Å.

They have used an electron spectrometer to demonstrate that certain photoelectrons released from the metal (as opposed to the oxide) during irradiation with $MgK\alpha_{1,2}$ X-radiation could not escape if the thickness of the oxide layer were any more than 15 ± 10 Å. The situation is illustrated in the diagram; the smaller peaks in *a* are caused by photoelectrons from the metal and the larger ones by electrons from the oxide layer. The spectra in *b* are for a piece of aluminium sheet that had been exposed to an atmosphere rich in oxygen for 3 min at 600° C. Further oxidation apparently proceeds smoothly.

Clearly the oxide film has increased in thickness to the extent that the photoelectrons from the metal can no longer escape. And Tripathi and Clark also point out that there is a shift in the position of the peak in the two situations, suggesting that when the oxide film is thick there is no longer any electrical contact with the spectrometer so the sample charges up.



The anomaly below the indentation. The crack can just be seen to its left. (From *J. Phys. D*, **6**, 117; 1972.)

from that piled up at the surface) has been transferred into the spherical volume, the calculated value of $\delta\rho/\rho$ is 3.2×10^{-2}. Puttick says, however, that the agreement between these values may be misleading, for experiments on hydrostatic compression of Perspex suggest that, at the maximum pressure of 3 kbar exerted in the indentation experiments, $\delta\rho/\rho$ should only be 3×10^{-4}. (But there is another *caveat* here, for the Perspex beneath the indenter has also undergone plastic flow).

QSOs

Redshifts and Distances

by our Cosmology Correspondent

Bahcall and Hills have investigated the magnitude-redshift relation for the QSOs which are most luminous optically in the redshift range from 0.2 to beyond 2.0. They have found that the distribution is entirely consistent with QSOs being at the cosmological distances indicated by a Doppler interpretation of their redshifts, participating in the overall expansion of the universe (*Astrophys. J.*, **179**, 699; 1973).

Efforts to resolve the nature of QSOs remain, of course, a continuing astronomical saga. With distance, velocity, absolute magnitude and mass all unknown, the problem of providing a fit between theory and observation is not difficult—but then the validity of any particular fit to the real universe is highly questionable. In some way, it is necessary to restrict the sample of QSOs being examined to, say, all those of a certain mass, at a certain distance, or of a certain brightness. Taking a leaf out of the textbook studies of clusters of galaxies, Bahcall and Hills have made the not unreasonable assumption that for any redshift z the brightest QSO that can be seen on Earth will have an intrinsic brightness close to some limiting upper value, and that it will thus provide a "standard candle". If the redshift provides a measure of distance, the apparent brightness of the appropriate standard candle will be less for larger z; more specifically, the exact relation between redshift and apparent magnitude will depend intimately on the properties of the Universe as a whole.

The data used in the latest analysis come from the catalogue of DeVeny *et al.* (*Publ. Astron. Soc. Pacific*, **83**, 611; 1971). Because it is important to use bins which contain the same number of QSOs, in order to have a sampling which is unbiased with respect to redshift, Bahcall and Hills have not divided the redshift range into equal increments Δz, but have taken bins of different Δz which each contain fifteen QSOs. There were 105 QSOs in the sample, filling seven bins and providing seven brightest QSOs as standard candles. These are, in order of increasing z and decreasing apparent magnitude, 3C 273, 3C 232, PKS 1354+19, PKS 1252+11, PKS 1127–14, 3C 298 and TON 1530.

Bahcall and Hills discuss likely sampling effects, such as the probability of their sample including a violently variable QSO which happened to be flaring when observed; in spite of these complications, they are able after careful statistical analysis to fit the seven QSOs to a straight line of slope 5 in the log$z$/apparent magnitude diagram. Two very large redshift QSOs which cannot be included in the statistical analysis because there are not enough QSOs known with $z>2.2$ to complete a fifteen member bin also lie close to this straight line (they are PHL 957, $z=2.69$, and 4C 05.34, $z=2.88$; if large redshift does indicate large distance, these must be equivalent to brightest member QSOs in order to be visible.

This evidence suggests that QSO redshifts are cosmological in origin and that there is no strong evolution of the luminosity of brightest member QSOs with cosmological epoch. Because of the wide range of redshifts covered in the analysis, this is a very powerful result. It remains possible—indeed probable—that in any group of QSOs the brightest member will not always be the same object; what the data reveal is that the physical properties of the Universe which define the brightness limits on the whole class of objects known as QSOs have remained roughly constant as the Universe itself has evolved.

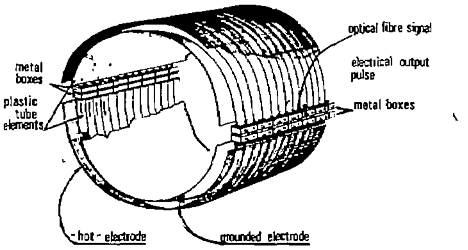
The analysis used by Bahcall and Hills is not limited to QSOs, however, and provides a tool which can be applied to the investigation of other objects which have a broad luminosity function and for which redshift measurements have been made.

Plastic Tubes as Particle Detectors

In next Monday's *Nature Physical Science* (February 26) Conversi, the founding father of the flash tube particle detector, a device beloved of cosmic-ray physicists, describes how these detectors can be made in a flexible form from plastic materials rather than glass. As is the case for the more conventional tubes, a voltage pulse is applied across a layer of the flexible detectors a microsecond or so after the registration of a charged particle by means of a logic system; those tubes through which the particle passed will then flash along their whole length. The tubes have to be protected from extraneous light, except at one end where recording can take place either by means of a flexible optical fibre or by a probe within each tube which can pick up a small voltage pulse.

Conversi describes a particular way in which the new detector could be used with the electron–positron storage ring at Frascati (see diagram). Conversi envisages that the 2 m "experimental" straight section of the storage ring would be surrounded by two layers of tubes (only one of which is shown in the diagram). With plastic tubes of diameter 1.6 cm, 500 tube elements would be needed to cover the whole section. The vacuum chamber of the storage ring could well be the inner grounded electrode and the high voltage ("hot") electrode would probably be a gauze to minimize Coulomb scattering of the charged particles.

One of the disadvantages of flash tubes as compared with, say, spark chambers is that several layers of parallel tubes will only locate the particle trajectory in two dimensions. If it is required to reconstruct particle interactions in three dimensions, then extra layers with the axes of the tube elements pointing in different directions—for example, parallel to the length of the vacuum chamber of the storage ring in Conversi's example—would have to be added.



In his experiments on the new device Conversi used a high voltage pulse about 5 μs long with a rise time of about 50 ns. The peak field was 8 kV cm^{-1}, and a mixture of neon (30 per cent) and helium (70 per cent) was pumped through the system at a rate of 1 $\text{cm}^3\ \text{s}^{-1}$.

Machines and the Theory of Intelligence

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This article is based on a series of special lectures delivered at University College, London, in November 1972.

THE birth of the subject generally referred to as "artificial intelligence" has been dated[1] from Turing's paper[2] *Intelligent Machinery* written in 1947. After twenty-five years of fitful growth it is becoming evident that the new subject is here to stay.

The scientific goal of research work in artificial intelligence is the development of a systematic theory of intelligent processes, wherever they may be found; thus the term "artificial intelligence" is not an entirely happy one. The bias towards artefacts is reminiscent of aerodynamics, which most people associate with aeroplanes rather than with birds (yet fruitful ornithological application has been achieved[3]). Here I shall review briefly some of the experimental knowledge systems which have been developed, and indicate how pieces of theory abstracted from these might fit together.

Some Performance Systems

Game playing was an early domain of interest, and Shannon[4], Turing[5], and Newell, Shaw and Simon[6] contributed classic analyses of how machines might be programmed to play chess. The first significant performance system was Samuel's program[7] for checkers, which eventually learned to play at the level of a good county player, far higher than that of Samuel himself. This last circumstance played a valuable part in discrediting the cruder manifestations of the doctrine that "you only get out what you put in".

The fundamental mechanism underlying all this work has been a cycle of processes: lookahead, evaluation and minimaxing. These derive ultimately from a method used to establish a "foregone conclusion theorem" for such games (two person, zero sum, perfect information, no chance moves) which states that the outcome value can be computed on the assumption that both players follow a (computable) best strategy. For a trivial game, such as that schematized in Fig. 1*a*, the computation can actually be performed: all terminal board positions are assigned values by the rules of the game, and these are "backed up" by the minimax assumption that White will always choose the immediately accessible position which has the maximum value and that Black will select the one with the minimum value. Clearly the procedure not only demonstrates a theorem but also defines a strategy.

But what is to be done when, as in any serious game, it is not practicable to look ahead to the end? Turing and Shannon independently suggested looking ahead as far as practicable, to what may be termed the "lookahead horizon", assigning some approximate values to the positions on the horizon by an evaluation function, and backing these up by the same minimax rule. The corresponding strategy says "choose that immediate successor which has the highest backed-up value".

This rule has been proved empirically in numerous game-playing programs, but in spite of its intuitive appeal it has never been formally justified. The question is posed diagrammatically in Fig. 1*b*.

Search procedures form part of the armoury of the operations-research man and the computer professional. Stemming from such work as Samuel's, people concerned with game playing and problem solving have implemented mechanisms for guiding the search, first, by forming sub-problems[8] or, second, by making heuristic estimates of distance-to-goal[9]. Various theorems have established conditions under which such techniques can be used without sacrificing the certainty of termination or the optimality of the solution found[10,12,13].

The use of an "evaluation function" to guide the search is a way of smuggling human *ad hoc* knowledge of a problem in through the back door. There is no cause to disdain such a route; it is after all one of the principal channels through which natural intelligences improve their understanding of the world. At the same time automatic methods have been developed for improving the reliability with which problem states are evaluated[11].

Samuel's early work on game learning[7] indicated that seemingly pedestrian mechanisms for the storage and recall

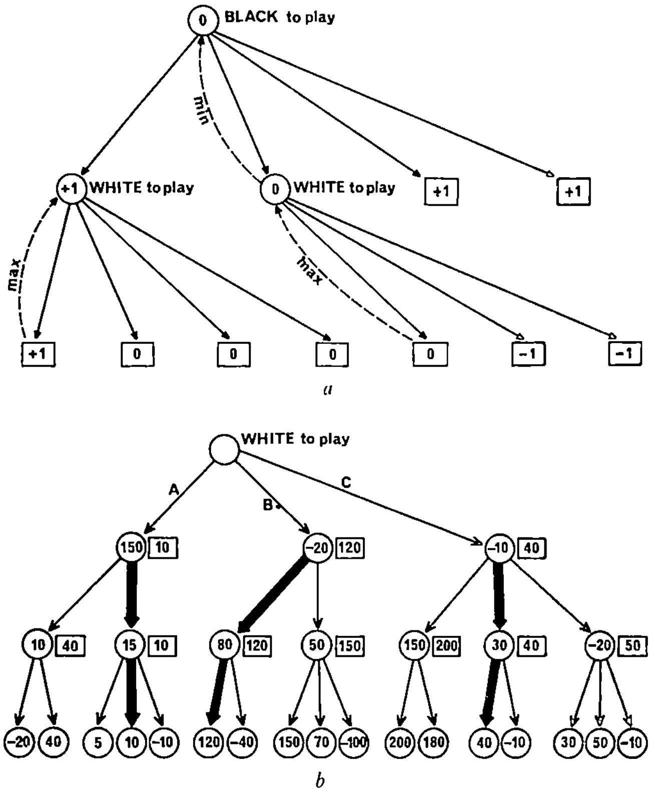


Fig. 1 *a*, The root of this two-level lookahead tree acquires a value by alternate application of the "max" and "min" functions. If alternation is extended backwards from all terminal positions of the game tree, the initial position of the entire game will ultimately be assigned a value. Terminal positions are shown as boxes; *b*, lookahead tree in which the nodes are marked with "face values". Boxed figures are values backed up from the lookahead horizon. If move-selection were decided by face values, then move A would be chosen, but if backed-up values then move B. What is the rationale for B ?

of previously computed results can have powerful effects on performance. Recently the combination of rote learning schemes with heuristic search has been shown to have applications to plan formation in robots[13,14]. To exploit the full power of this combination, whether in game playing, in robotics or in other applications, one would like the rote dictionary to contain generalized descriptions or "concepts" (for example, of classes of game-positions "essentially similar" from a strategic point of view) to be looked up by processes of recognition, rather than by point-by-point matching. Such a dictionary is to be used in the style "If the situation is of type A, then perform action x, if of type B, then action y" and so on. One is then in effect processing a "decision table" which is formally equivalent to a computer program. There is thus a direct link between work on the automatic synthesis of strategies in game playing and robotics, and work directed towards automatic program-writing in general.

Recognition usually involves the matching of descriptions synthesized from sensory input with stored "canonical" descriptions of named objects, board positions, scenes, situations and so on. Choice of representation is crucial. At one extreme, predicate calculus[15] has the merit of generality, and the demerit of intractability for updating and matching descriptions of objects, positions, scenes or situations; at the other extreme lie simple "state vector" representations, which fall down through awkwardness for handling complex interrelationships. Somewhere in the middle lies the use of directed labelled graphs ("relational structures", "semantic nets") in which nodes stand for elements and arcs for relations. Impressive use of these structures has been made in a study of concept formation in the context of machine vision[16].

Language interpretation has been the graveyard of many well-financed projects for "machine translation". The trouble proved to be the assumption that it is not necessary for the machine to "understand" the domain of discourse. One of the first demonstrations of the power of the semantic approach in this area was Bobrow's "STUDENT" program[17] for answering school algebra problems posed in English. A program by Woods, Kaplan and Nash-Webber[18] for the interrogation in English of a data base with a fixed format has been used by NASA scientists to answer questions about Moon rocks. An essay by Winograd[19] on computer handling of English language dialogue, again making intensive use of an internal model of the dialogue's subject matter, has left no doubt that machine translation can only be solved by knowledge-based systems. The knowledge base required to render arbitrary texts non-ambiguous is now recognized to be bounded only by the knowledge possessed by their authors. Winograd compares the following two sentences:

The city councilmen refused to give the women a permit for a demonstration because they feared violence.

The city councilmen refused to give the women a permit for a demonstration because they advocated revolution.

The decision to refer "they" to "councilmen" in the first case and to "women" in the second implies a network of knowledge reaching into almost every corner of social and political life.

Mass spectrogram analysis was proposed by Lederberg as a suitable task for machine intelligence methods. The heuristic DENDRAL[20] program developed by him and Feigenbaum now outperforms post-doctoral chemists in the identification of certain classes of organic compounds. The program is a rich quarrying ground for fundamental mechanisms of intelligence, including the systematic conjecture of hypotheses, heuristic search, rote learning, and deductive and inductive reasoning. I shall refer back to this work later in connexion with the use made by intelligent systems of stored knowledge.

Of all the knowledge systems which have been attempted, robotics is perhaps the most simple in appearance. In reality, however, it is the most complex. The chess amateur can appreciate that Grandmaster chess has depth and subtlety. But there is no such thing as a human amateur at tasks of navigation and "hand-eye" assembly. Every man is a Grandmaster at these tasks, having spent most of his waking life in unwitting but continual practice. Not having been informed that he is a Grandmaster, and having long since stored most of his skill at a subliminal level, he thinks that what seems subjectively simple is objectively so. Experience of research in robotics is a swift and certain cure. Something of the depth of analysis which is required can be gleaned from the discussion by McCarthy and Hayes[21] of the properties which should be possessed by a calculus of situations, actions and causal laws.

The crux of any such calculus is how to represent in a formal language what the robot knows about its world. McCarthy and Hayes distinguish "epistemologically adequate" and "heuristically adequate" representations. (In an earlier generation Ryle[22] contrasted "knowing that" and "knowing how".) "The epistemological part is the representation of the world in such a form that the solution of problems follows from the facts expressed in the representation. The heuristic part is the mechanism that, on the basis of the information, solves the problem and decides what to do."

I shall consider now what is probably the simplest world to be seriously discussed, that of Popplestone's "blind hand" problem (internal report, Department of Machine Intelligence, Edinburgh), with the object of indicating that there is more to robot reasoning than meets the eye, and expanding a little the epistemological-heuristic distinction.

A blind, insentient, robot shares with one or more "things" a world consisting of only two places "here" and "there", and has available to it the actions "pickup", "letgo" and "go". "Pickup" is non-deterministic and causes (if the hand is empty when the action is applied) a "thing" selected at random from the place where the robot is, to acquire the property "held". An initial situation called "now" is defined, in which it is asserted that every thing at "here" (and there is at least one such) has the property "red". A goal situation is defined as one in which at least one red thing is at "there".

Invariant Facts and Laws

The kinds of facts which the robot needs to know include that the robot and anything held by it must be in the same place, and that something cannot be in both places at once. Using a prescription of Green[23], a formalization of this apparently trivial problem in first order logic might start along the following lines. (The variables t, p and s are to be interpreted as standing for objects, places and situations respectively.)

for all t,p,s: held(thing(t),s) and at(thing(t),p,s) implies at(robot,p,s),

for all t,p,s: held(thing(t),s) and at(robot,p,s) implies at (thing(t),p,s),

for all p,s: at(robot,p,s) implies at (thing(taken(s)),p,s),

for all t,s: at (t, here,s) implies not at (t, there, s).

The conjunction of these statements describes some of the physics of this world. The last statement, for example, asserts that an object cannot be both at "here" and at "there" in one and the same situation.

The initial situation, "now", is described in like manner:

for all t: at (t, here, now) implies red(t), at(thing (a), here, now).

The latter statement merely asserts that at least one thing (represented by the constant a) is at "here" in situation "now". The function "thing" is a convenience for distinguishing other objects from the robot, whom we may wish to exclude from some otherwise universal statements—like one implying that the robot is "held", for instance.

How can the machine be enabled to reason about the chains of possible consequences derivable from "now" and so to construct an action chain leading to a goal situation? The goal may be defined, using Green's "answer" predicate[24], as:

for all t, s: at(t, there, s) and red(t) implies answer(s).

But how do we handle the actions? The contrast between epistemological and heuristic criteria becomes very sharp at this point. Consider two approaches.

One can go the whole way and stick to formal logic, defining the transition laws of our world under the various actions. For example, the first of the following three "letgo" axioms translates freely: "in the situation produced by doing a 'letgo', nothing is held".

for all *t*, *s*: not held (thing(*t*), do(letgo, *s*)),

for all *t*,*p*,*s*: at(*t*,*p*,*s*) implies at(*t*, *p*, do(letgo, *s*)),

for all *t*,*p*,*s*: not at(*t*,*p*,*s*) implies not at(*t*,*p*,do(letgo, *s*)),

and similarly for the other actions.

Now the problem of plan construction is reduced to one of logical deduction, in fact deduction of the statement "answer(do(go(there), do(pickup, do(go(here), do(letgo, now)))))". This says, in English, that "the goal situation is the one resulting from doing a "go there" in the situation resulting from doing a "pickup" in the situation resulting from doing a "go here" in the situation resulting from doing a "letgo" in the situation "now" ", and it is clear how this can be re-interpreted as an algorithm.

This deduction can in principle be mechanized, but there are two severe snags. First, the need to incorporate "frame axioms"[24,25] (which spell out all the facts which remain unchanged after the performance of given actions, as in the last logic statement above) escalates for nontrivial problems and renders the automatic deduction process intractable even in the present toy problem. Second, the logic representation is not heuristically adequate.

On the other hand, one can go to the other extreme, and express the whole problem as a computer simulation couched in a suitable programming language, matching situations with data structures and actions with procedures. But this approach encounters difficulties with the epistemological criterion, for the structure of the problem world can be readily complicated so that it can no longer easily be described by the use of simple representations of the "state vector" type. Various attacks are being made on the representation problem in an attempt to make the best of both worlds, the epistemological and the heuristic. Some good early suggestions were made by Popplestone, using essentially the same blind hand problem, and were reviewed in *Nature*[27] two years ago. Since then powerful new programming aids, such as the PLANNER[28], QA4 (ref. 29) and CONNIVER[30] languages have come into play. In addition particular mention should be made of the Stanford Research Institute's study of autonomous plan formation[14,15], in which many of the matters discussed above have been under experimental investigation.

The key ideas on which much work centres is that plan construction should be conceived as a search through a space of states of knowledge to generate a path connecting the initial knowledge state to one which satisfies the goal definition. Everything turns on finding ways of representing knowledge states so that the transformation of one into another can be neatly computed from the definition of the corresponding action ("What will I know about the state of affairs after doing A ?").

Experimental Robotics

The STRIPS system[14,15] at Stanford Research Institute combines reasoning in first-order predicate calculus with heuristic search. In the situation depicted in Fig. 2 the robot must devise a plan for pushing objects around so that one of the boxes end up in room R1, subject to the constraint that at no time must the wedge be in the same room as a box. If the plan goes wrong, the system must be capable of recovering from error state and, if possible, "mending" the failed plan appropriately. Facilities are incorporated whereby successful plans are automatically "remembered" and their elements recombined for use in appropriate future situations[14].

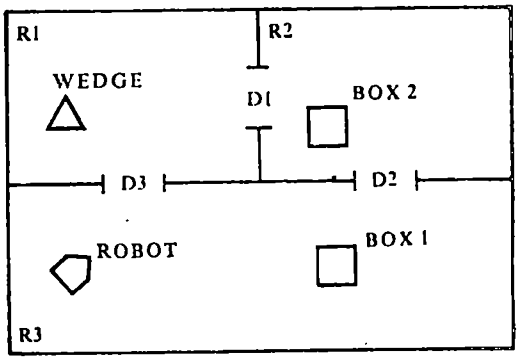


Fig. 2 Robot environment for a constraint problem. (Reproduced from ref. 31.)

Following simultaneous development of the idea of optical ranging in Japan[32], Britain (R. J. Popplestone, personal communication) and America[33], Stanford University's robot project uses a laser optical ranging system for mapping the three-dimensional surfaces of "seen" objects. Another branch of the same project is currently able to assemble an automobile water pump comprising two pieces, a gasket and six screws (J. Feldman, personal communication). This is done blind, using mechanical feedback.

At Edinburgh automatic assembly is also under study. Programs exist for packing simple objects onto a confined surface, identifying a limited set of objects by visual appearance, and solving problems of stacking rings on pegs (D. M., A. P. Ambler, H. G. Barrow, R. M. Burstall, R. J. Popplestone, and K. J. Turner, paper to be presented at a Conference on Industrial Robot Technology at the University of Nottingham next month).

In industrial laboratories, notably in America (for example, the Charles Stark Draper Laboratory of MIT) and Japan[34], automatic assembly studies are multiplying.

Idea of a Theory

I have already mentioned the abstracting of pieces of theory from performance systems such as those listed above. What is meant by "theory" in this context ? I have just considered a fragment of simple robot world theory, and one can, of course, speak of a piece of chess end-game theory (for example, that expressed by Tan's program[35] for the two-Kings-and-one-Pawn end-game) or of the theory of mass spectrometry embedded in the heuristic DENDRAL program. One can even, legitimately, speak of Winograd's program as constituting a linguistic theory, or at least as containing or implying one. But these theories are descriptive of specific domains, not of intelligence itself.

It would be naive to pretend that the search for a metatheory is something new, or even that it is anything but old philosophy in new dress. An early name suggested for what is now "artificial intelligence" was "epistemological engineering" (P. M. Woodward, personal communication). The new epistemology, however, has a trick which the old philosophers lacked, namely to express any given theory (of knowledge, reasoning, abstraction, learning and the like) in a sufficiently formal style to program and test it on the machine.

Hence there is no longer a meaningful distinction to be drawn between a theory of some given intelligent function, and an algorithm for carrying it out (which could in turn be converted into a program for some particular machine) together with any useful theorems for describing the algorithm's action. Algorithms, then, are theories, and this has been true for a long time. But there have been no reasonable mechanisms available for handling them. Mathematics, on the other hand, has had the necessary mechanisms for manipulating the formalisms which it uses for describing physical systems. Hence closed-form mathematics has been the "typical" embodiment of theory in the physical sciences. By contrast, the "typical" embodiment of theory in cognitive engineering is algorithmic.

What Use is Knowledge?

The value of stored knowledge to a problem-solving program again divides into epistemological and heuristic parts. In the first place sufficient knowledge must be present for solutions to be in principle deducible. But that is only the start. Heuristically, the value of knowledge is that it offers ways of avoiding, or greatly reducing, processes of search. The natural enemy of the worker in the field of artificial intelligence is the "combinatorial explosion", and almost his entire craft is concerned with ways of combatting it. The following three examples illustrate the use of stored knowledge to damp off combinatorial explosions.

First, Tables 1 and 2 show the number of combinatorially possible ways in picture-processing of labelling various patterns of intersecting lines, contrasted with the number that are physically possible on the assumption that they arise in retinal projections of three-dimensional scenes composed of plane polyhedral bodies, such as that shown in Fig. 3*a*. The computer program achieves this order of reduction by the use of an appropriate theory. Here I shall review briefly a subset of the theory, adequate for interpreting line drawings of plane-surfaced polyhedra, with trihedral vertices only and without shadows. In this way the flavour can be imparted of the kind of reasoning involved in more complex cases.

Each line in such a drawing can be assigned to one or another of various possible causes: it corresponds to a convex edge, a concave edge, or to an edge formed by two surfaces, only one of which is visible. A corresponding label can be attached to each line, as has been done in Fig. 3*b* using Huffman's conventions[36]. The remarkable fact emerges from Huffman's analysis that only a few of the combinatorially possible ways of labelling such drawings correspond to physically possible structures in the outside world: only twelve distinct configurations of lines around vertices are possible. A computer program can use the theoretical constraints to process the picture, by searching through the space of possible labellings for those which are legal (that is, do not entail that any line should receive two different labels) under the constraints.

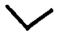
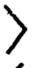
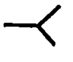
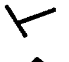
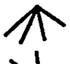
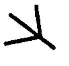
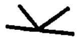
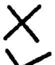
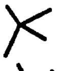
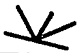
Second, Table 3 contrasts the number of topologically possible molecular graphs corresponding to given empirical formulae with the number of candidate interpretations remaining after the Heuristic DENDRAL program has applied its stored theory of chemical stability. The program constructs, using evidence of various kinds, a "GOODLIST" of substructures which must appear in any structure hypothesized by the program and a "BADLIST" of substructures which must not appear. As a simple example, at a given stage down a search tree might be the partial hypothesis —CH_2—O—CH_2— and a possible next move for the structure-generator procedure might be to attach a terminal carbon, forming —CH_2—O—CH_2—CH_3. But unless the data contains peaks at 59 and at M-15 this continuation is forbidden. Again, the structure-generator can be made to handle as a "super-atom" a fragment indicated by the mass spectrum. Additional opportunities to do this arise when the presence of methyl super-atoms can be inferred from nuclear magnetic resonance data, when available.

Table 1 A Labelling Scheme

+	1 Convex edge
→	2 Obscuring edges—obscuring body lies to right of arrow's direction
←	3
→c	4 Cracks—obscuring body lies to right of arrow's direction
←c	5
↑	6 Shadows—arrows point to shadowed region
↓	7
−	8 Concave edge
$\overset{-}{\rightarrow}$	9 Separable concave edges—obscuring body lies to right of arrow's direction—double arrow indicates that three bodies meet along the line
$\overset{-}{\leftarrow}$	10
$\overset{-}{\times}$	11

Reproduced from ref. 42.

Table 2 Comparison of Number of Combinatorially Possible Labellings with the Number that are Physically Possible

	Approximate number of combinatorially possible labellings	Appoximate number of physically possible labellings.
	2,500	80
	125,000	70
	125,000	500
	125,000	500
	6×10^6	10
	6×10^6	300
	6×10^6	100
	6×10^6	100
	6×10^6	100
	3×10^8	30

Reproduced from ref. 42.

Third, McCarthy's problem of the multilated checkerboard[37] is quintessential to the point here discussed. The squares at opposite corners of an 8×8 checkerboard are removed, leaving sixty-two squares. Thirty-one dominoes are available, each of such a size and shape as to cover exactly two adjacent squares of the checkerboard. Can all the sixty-two

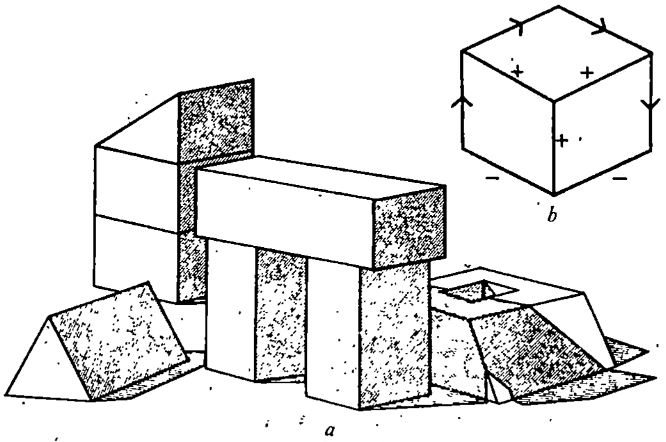


Fig. 3 *a*, A complex three-dimensional scene; *b*, Huffman labels for a cube. Plus implies a convex edge, minus implies concave, and an arrow implies that only one of the edge-forming surfaces is visible.

Table 3 Comparison of the Number of Topologically Possible Molecular Graphs Corresponding to Given Empirical Formulae with the Number of Candidate Interpretations Remaining after the Heuristic DENDRAL Program has Applied its Stored Theory of Chemical Stability

		Number of isomers	Number of inferred isomers	
			A	B
Thiol	1-nonyl	405	89	1
	n-decyl	989	211	1
	n-dodecyl	6,045	1,238	1
Thioether	di-n-pentyl	989	12	1
	di-n-hexyl	6,045	36	1
	di-n-heptyl	38,322	153	1
Alcohol	n-tetradecyl	38,322	7,639	1
	3-tetradecyl	38,322	1,238	1
	n-hexadecyl	151,375	48,865	1
Ether	Di-n-octyl	151,375	780	1
	bis-2-ethylhexyl	151,375	780	21
	di-n-decyl	11,428,365	22,366	1
Amine	n-octadecyl	2,156,010	48,865	1
	N-methyl-n-octyl-n-nonyl	2,156,010	15,978	1
	N,N-dimethyl-n-octadecyl	14,715,813	1,284,792	1

A, Inferred isomers when only mass spectrometry is used; B, inferred isomers when the number of methyl radicals is known from nuclear magnetic resonance data. Based on ref. 20.

squares be exactly covered by some tessellation of the thirty-one dominoes ?

However sophisticated the search procedure which a heuristic program might use to attack this problem by trial and error, the combinatorics of the problem will defeat it. If the reader is unsure of this, let him mentally enlarge the board to, say, 80×80, or $10^8 \times 10^8$. But so long as the dimensions of the board are both of even, or both of odd, length (such boards are called "even" boards) then the problem stays the same for any solver armed with certain crucial pieces of knowledge, namely: that the two squares which are removed from opposite corners of an even board must be of the same colour, and that each domino must cover exactly one white and one black square. The problem now falls apart. The mutilated checkerboard cannot be covered.

To discover formal schemes within which such key facts can automatically be mobilized and their relevance exploited in an immediate and natural fashion is closely bound up with what was earlier referred to as "the representation problem". A familiar example is that certain representations of the game of Nim trivialize the calculation of a winning strategy; but the program capable of inventing such representations is yet to be devised.

Progress Towards an ICS

Two years ago I discussed in *Nature*[27] the possibility of implementing in software an Integrated Cognitive System (ICS). The attainment on a laboratory scale of a "working model", it was suggested, could be used as an indicator of ultimate feasibility. A working model of an ICS, as a minimal set of requirements, should be able: to form an internal representation of its task environment, summarizing the operationally relevant features; to use the representation to form plans of action, to be executed in the task environment; to perform directed perceptual sampling of the environment to switch execution along conditional branches of the plan; to recover from error state when execution fails; to cope with complex and ill-structured environments; to be told new goals and to work out its own approaches to them; and to use the record of past failures and successes to revise and extend the representation inductively.

A computer program which was not able to do most of the above, however excellent a feat of software technology it might be, would not count as an artificial intelligence program. The guidance software for the Apollo on-board computer, written for NASA by Draper Laboratories (J. Moore, privately circulated report, Department of Computational Logic, University of Edinburgh) and charged with the task of getting the spacecraft to the Moon and back, is disqualified on this criterion. On the one hand, it is an acknowledged masterpiece, and on the other, in common with other and lesser automatic control systems, it scores a significant mark only for the third item in the above list.

The on-board computer does not need to plan because hand-coded routine have been provided for all probable situations—analogous, perhaps, to the elaborate, but essentially reflex, nervous system of an insect. The reason for regarding the Apollo on-board system as sub-intelligent is thus concerned with the nature of the internal model which it has of its environment. More than a quarter of a century ago Craik[38] first called attention to the crucial role in thought and perception of internal models. The world of the Apollo computer is so simple and determinate that its behaviour can be completely characterized by computationally simple equations. These equations, which comprise the system's "internal model" in Craik's sense, capture the dynamics of all possible configurations of the objects of its world, and supply all information needed about their interactions and properties.

But consider the mission: not to go to the Moon and back, but the much harder one of going down to the tobacconist and back. By contrast with the space mission, the task environment is exceedingly complex and "messy" and the unexpected lurks at every point of the route (the stairs may be swept, unswept, blocked . . . , the front door may be open, shut, locked . . . , the weather may be bright, dull, wet, windy . . . and so on). Alternatively, and only a little less taxing (at least the environment does not contain other autonomous beings to worry about), consider the mission of a Mars Rover vehicle, such as that already envisaged by NASA[39] and by the space section of the USSR Academy of Sciences (N. Zagoruiko, personal communication). Arising from the fact that it is not possible to pre-program solutions to all problems which might arise while exploring an unknown terrain, a specific ten-year programme of machine intelligence research is regarded as a necessary preliminary condition for putting such operational vehicles into commission. Note that if such a vehicle is to handle all the tasks of autonomous exploration, and assembly and use of instruments, which will be demanded of it, then it must score seven out of seven on the criteria posed earlier.

That achievement lies in the future. How do matters stand today with regard to "working models" ? Each of the seven capabilities listed can now be found in one or another experimental system, and there are some systems which exhibit many, or even most, of them. Unfortunately the most interesting capability of all, central to the phenomenon of intelligence, is the one which is still the least well understood—namely inductive generalization. Yet significant progress has been made[16,40].

In summary, incomplete systems are becoming commonplace and complete "working models", at the most primitive level, now seem not very far off. The likely technological lag before such systems might be upgraded to near-human intellectual performance is a topic for separate consideration.

Implications and Forecasting

It would plainly be desirable to find some objective basis for predicting the rate of development and social impact of machine intelligence. An objective basis is lacking at present and it is only possible to record samples of subjective opinion and to categorize lines of enquiry which more objective studies might follow. Fig. 4 summarizes some of the results of an opinion poll taken last year among sixty-seven British and American computer scientists working in, or close to, the machine intelligence field.

In answer to a question not shown in Fig. 4, most considered that attainment of the goals of machine intelligence would cause human intellectual and cultural processes to be enhanced rather than to atrophy. Of those replying to a question on the risk of ultimate "takeover" of human affairs by

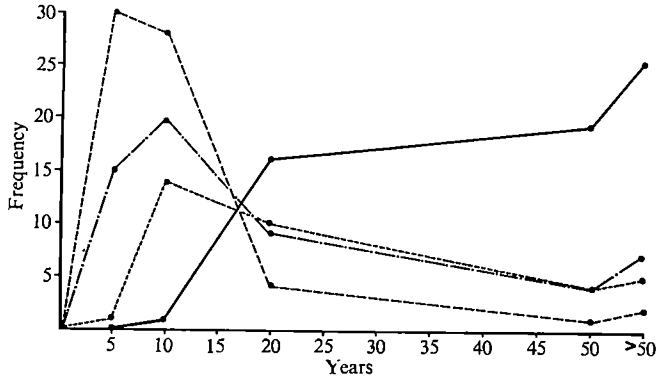


Fig. 4 Opinion poll on machine intelligence. Estimated number of years before: ——, computing system exhibiting intelligence at adult human level; – – –, significant industrial spin-off; —·—, contributions to brain studies; - - -, contributions from brain studies to machine intelligence.

intelligent machines, about half regarded it as "negligible", and most of the remainder as "substantial" with a few voting for "overwhelming".

A working party recently convened under the auspices of the Rockefeller Foundation at Villa Serbelloni, Lake Como, on June 11 to 15, 1972, considered the gradations through which complex information systems might evolve in the future, ranging from contemporary industrial control systems, and "data look-up" retrieval, to autonomous computer networks developed for controlling urban functions (telephones, electricity distribution, sewage, traffic, police, banking, credit systems, insurance, schools, hospitals, and so on). The backbone of such systems will develop anyway, by straightforward elaboration of conventional computing technology, including the integration of the various computational networks into total systems. It seems likely that such systems will also ultimately incorporate autonomous planning and decision-taking capabilities, derived as "spin-off" from developments based on artificial intelligence in, for example, space and oceanographic robotics. A danger could then arise of city dwellers becoming dependent on systems which could no longer be fully understood or controlled. Counter-measures to such dangers might include the introduction of auditing procedures for computer programs, research on program-understanding programs, and system-understanding systems generally, and, finally, the advent of programs to teach the users of intelligent systems.

On the other side of the balance sheet, the working party took preliminary note of several anticipated benefits. The mechanization of industrial production has been associated in the past with the imposition of a deadening uniformity of design. Automated intelligence in the factory could offer the possibility of restoring the diversity and the "one off" capability originally associated with human craftsmanship. Related to this is the introduction of computer aids for the artist, composer, writer, architect and mathematician. Even the ordinary hobbyist might be enabled to perform feats which would today seem daunting or bizarre—building his own house, publishing his own writings, for example. The possible effects on computer-aided education have been stressed by others[41]: advances in this area will be of value not only to the young but also to older people as a means of acquiring new skills.

The formulation of an outline scheme of topics, and the compilation of relevant documents, represents an early stage of a study expected to occupy a number of years. Technical developments which occur in the intervening period will doubtless give such studies a firmer basis.

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Gravitational Waves and Relativistic Disks

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Relativistic disks enhance the intensity of radiation in directions near their plane. The gravitational pulses which Weber claims to have detected may arise in such a disk situated in the Galactic nucleus, with its plane aligned with that of the Galaxy. A typical enhancement factor is 30.

It seems improbable that an isotropic source of gravitational radiation situated at the Galactic centre can be responsible for the gravitational events observed by Weber[1]; that would require embarrassingly high mass-loss rates (perhaps as high as $10^4\ M_\odot\ \mathrm{yr}^{-1}$). Misner[2] has suggested that the radiation is produced by a gravitational synchrotron process, giving rise to narrowly beamed radiation confined to the plane of the Galaxy. But Davis *et al.*[3] have concluded, on theoretical grounds, that such beaming would not occur to the required extent in the process envisaged by Misner. I describe here another model of anisotropic emission.

Relativistic disks are flat, strongly self-gravitating systems of particles or material, collapse of which is prevented by rapid rotation. As objects of possible astrophysical interest, they have been the object of much recent research[4–6]. My suggestion is that the Galactic nucleus contains a relativistic disk whose plane coincides with that of the Galaxy, and that gravitational radiation is generated at a "reasonable" rate within the disk. I show that the intensity is enhanced in directions near to the plane of the disk by the latter's gravitational field. A typical enhancement factor is ~ 30, and possibly higher. The radiation might be generated in such a system by gravitational encounters between the particles (for example, neutron stars or black holes) composing it, or by accretion of these particles by a massive black hole at the centre of the disk. The latter possibility has an attractive feature, namely that Misner's mechanism, and the one described here would operate simultaneously, the two effects combining multiplicatively.

The Enhancement Factor

As an illustration, I consider a locally isotropic source of radiation situated at the centre of the disk. I use geometrical optics, which turns out to be reasonable if the radius R of the system $\gg 100\ \times$ the wavelength λ of the waves detected by Weber, that is, $R \gg 2 \times 10^4$ km. A ray leaving the centre C at a small angle α_i to the disk plane (see Fig. 1) can cross and re-cross the disk many times before escaping at an angle β to the plane; α_f is the crossing angle at the last crossing point P. (Transparency of the disk material to gravitational waves is quite justifiable, and in any case a disk composed of particles would almost certainly be optically thin.) I make the not unduly restrictive assumption that the surface density of the disk material decreases with increasing distance from the centre, in which case the inequalities $\alpha_i > \alpha_f \gtrsim \beta$ hold (that is, regarding all angles as positive.) It is the fact that most rays have an escape angle β smaller than the starting angle α_i which is responsible for the intensity enhancement.

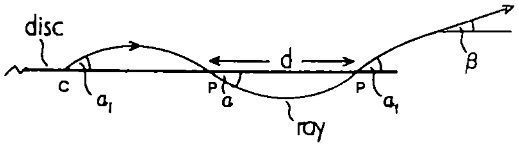

Fig. 1 A typical ray path.

Corresponding to a given β, there is a discrete set $(\alpha_{i,n})$ of values of α_i, each α_i corresponding to a given number n of crossing points. The smallest $\alpha_{i,n}$ $(\alpha_{\min})$ will correspond to the largest number $n_{\max}$ of crossing points, and to the smallest $\alpha_{f,n}$, which, from the above inequality, is approximately equal to β. The enhancement factor A is given by

$$A = \sum_{n=1}^{n_{\max}} \left| \frac{\mathrm{d}\alpha_i}{\mathrm{d}\beta} \right|_{\alpha_i = \alpha_{i,n}}$$

In order to estimate A, I consider an infinitesimally thin Newtonian disk with surface density $\sigma(\rho)$, a function of the distance ρ from the centre. I shall give an indication of the modification to be expected from general relativity later. Ray paths are given by the orbits of particles moving with speed c. If z is the height above the disk plane, the local path of a radial ray crossing the disk at some point $\rho = \rho_0$ and small angle $\alpha = \alpha_0$ is given by

$$\frac{\mathrm{d}^2 z}{\mathrm{d}t^2} \sim -2\pi G(\sigma_0 + \sigma_0' x)$$

and

$$\frac{\mathrm{d}x}{\mathrm{d}t} \sim c$$

where the prime denotes a ρ derivative, and $x = \rho - \rho_0$. Eliminating t between these equations, and integrating

$$z \sim \alpha_0 x - \frac{\pi G \sigma_0 x^2}{c^2}\left(1 + \frac{\sigma_0'}{\sigma_0}\frac{x}{3}\right)$$

The ray thus returns to the disk at

$$x \sim \frac{c^2\alpha_0}{\pi G\sigma_0}$$

and at a crossing angle

$$\alpha_0+\delta\alpha_0 \sim \alpha_0\left(1+\tfrac{1}{3}\,\frac{c^2\alpha_0}{\pi G\sigma_0}\,\frac{\sigma_0'}{\sigma_0}\right)$$

The crossing angle α and distance d between crossing points can be treated as continuous functions of ρ if $d \ll R$, which is the case of interest here. I have $d\sim c^2\,\alpha/\pi G\sigma$, and the above equation gives an estimate of α'

$$\frac{\alpha'}{\alpha} \sim \frac{\delta\alpha}{\alpha d} \sim \tfrac{1}{3}\,\frac{\sigma'}{\sigma}$$

giving

$$\alpha \sim \alpha_i\left(\frac{\sigma}{\sigma_i}\right)^{\frac{1}{3}}$$

and

$$d \sim d_i\left(\frac{\sigma_i}{\sigma}\right)^{\frac{2}{3}}$$

where the subscript i refers to values at $\rho=0$. These confirm that if $\sigma'<0$, α diminishes as we move towards the edge of the disk, and d increases. The ray will escape at a value of σ corresponding to $d\sim R$, the final crossing angle being

$$\alpha_f \sim \alpha_i\left(\frac{d_i}{R}\right)^{\frac{1}{2}} \sim \alpha_i\left(\frac{c^2\,\alpha_i}{\pi G\sigma_i R}\right)^{\frac{1}{2}}$$

This equation can be solved for $\alpha_{\min}$, the smallest α_i corresponding to a given β, which is given by $\alpha_f\sim\beta$. Thus

$$\alpha_{\min} \sim \left(\frac{\pi G\sigma_i R}{c^2}\right)^{\frac{1}{3}}\beta^{\frac{2}{3}}$$

The number of crossing points is $n\sim R/d_i\sim\pi G\sigma_i R/c^2\alpha_i$, so that

$$n_{\max} \sim \left(\frac{\pi G\sigma_i R}{c^2\beta}\right)^{\frac{2}{3}}$$

and

$$\alpha_{i,n} \sim \frac{\pi G\sigma_i R}{c^2 n}$$

In order to estimate $\mathrm{d}\alpha_i/\mathrm{d}\beta$, I note that when α_i changes from $\alpha_{i,n}$ to $\alpha_{i,n+1}$, β sweeps through a range $\sim\alpha_{f,n}$. Thus

$$\left|\frac{\mathrm{d}\alpha_i}{\mathrm{d}\beta}\right|_{\alpha_i=\alpha_{i,n}} \sim \frac{\alpha_{i,n}-\alpha_{i,n+1}}{\alpha_{f,n}} \sim \frac{1}{n^{\frac{1}{2}}}$$

Finally, I conclude that

$$A\sim \sum_{n=1}^{n_{\max}}\frac{1}{n^{\frac{1}{2}}} \sim 2n_{\max}^{\frac{1}{2}} \sim 2\left(\frac{\pi G\sigma_i R}{c^2\beta}\right)^{\frac{1}{3}}$$

A has its maximum value of $2\,\beta^{-\frac{1}{3}}$ in the extreme relativistic limit, when $\pi G\sigma_i R/c^2\sim 1$. The Solar System is about 10 kpc from the Galactic centre, and 4 ± 12 pc above the plane[7], giving $\beta\sim 10^{-3}$–10^{-4} rad, and in the above limit $n_{\max}\sim 10^2$–5×10^2 and $A\sim 20$–40. The mass-loss rate is reduced to roughly 300 $M_\odot$ yr^{-1}, which is just about compatible with the observational upper limit of 200 $M_\odot$ yr^{-1} averaged over the past 10^8 yr obtained by Sciama, Field, and Rees[8]. This mass-loss rate is still high in the sense that a galactic mass ($\sim 10^{11}$ $M_\odot$) would disappear in 10^8–10^9 yr. An interesting feature of enhancement factors ~30 is that the mass loss per event is reduced to about one solar mass. The requirement $d_i\gg\lambda$ when $\alpha_i=\alpha_{\min}$ gives the geometrical optics condition $R \gg \alpha_{\min}^{-1}\lambda \sim 100\lambda$ in this case.

The above result would allow $A\rightarrow\infty$ as $\beta\rightarrow 0$. But the finite thickness T of a real disk would intervene to prevent this, because for sufficiently small values of α rays would not rise out of the disk material, and would only enter vacuum on reaching the rim of the disk. The height $z_{\max}$ to which a ray rises above the plane is given by

$$z_{\max} \sim \frac{c^2\alpha^2}{4\pi G\sigma}$$

The requirement that this be greater than $T/2$, when $\rho=0$ and $\alpha=\alpha_{\min}$, gives $T/R<\beta/A$ as an approximate sufficient condition for the finite thickness not to be the limiting factor. Thus only thin disks ($T/R<10^{-5}$) can lead to the amplifications mentioned above. Such systems would almost certainly be unstable with respect to fragmentation[6], but probably only in the sense that flat galaxies develop a spiral structure. The thickness is determined by the particle mean square velocity v^2 perpendicular to the disk plane, the relationship being $T/R \sim v^2/c^2$ in the extreme relativistic limit. Thus $v/c<3\times 10^{-3}$.

A possible objection to the model is that Weber detects pulses of radiation, with pulse length[9] <0.5 s. The different path lengths involved here would tend to smear out a pulse; the overall path difference is of order $\alpha^2_{\min}\,R\sim A^2\beta^2 R/4$. Taking $\beta=3\times 10^{-4}$ rad and $A=30$, the above pulse length gives an upper limit of about 10^{10} km for the radius R. The corresponding upper mass limit is of order 3×10^9 $M_\odot$.

General Relativistic Modifications

The solution of Einstein's vacuum field equations which describes the gravitational field of a static infinitesimally thin homogeneous sheet, situated at $z=0$, is the metric

$$\mathrm{d}s^2=Z^{-2}\mathrm{d}t^2-Z^4(\mathrm{d}x^2+\mathrm{d}y^2+\mathrm{d}z^2)$$

where $Z=1-2\pi\sigma|z|$ (units in which $G=c=1$ are used here). This is a form of the Kasner solution[10]. The event horizons at $z=\pm 1/2\pi\sigma$ correspond in the Newtonian case to surfaces from which falling particles would reach the sheet with the velocity of light. It is instructive to compare null geodesics in this space-time with the corresponding Newtonian ray paths. A null geodesic in the plane $y=0$, leaving the origin at angle α to the sheet, obeys the equation

$$\frac{\mathrm{d}x}{\mathrm{d}z}=\frac{\cos\alpha}{(Z^6-\cos^2\alpha)^{\frac{1}{2}}}$$

When α is small, which is the case of interest here, we have $2\pi\sigma|z|\leq\alpha^2/6\ll 1$. This equation then integrates to

$$x\sim\frac{1}{6\pi\sigma}(\alpha-(\alpha^2-12\pi\sigma z)^{\frac{1}{2}})$$

so that the ray returns to the sheet at $x\sim\alpha/3\pi\sigma$. The maximum height above the plane is $z_{\max}\sim\alpha^2/12\pi\sigma$. Comparing these with the Newtonian values, Newtonian theory underestimates the pull of the sheet by a factor of 3.

Another non-Newtonian effect which has been ignored is that due to the rotation of the disk. This would make the rays spiral out from the centre, and thus increase the effective radius of the disk.

These considerations suggest that the Newtonian enhancement factors are somewhat pessimistic.

It is difficult to know what to call a reasonable mass-loss rate for the Galaxy in this context, but 10^{10} $M_{\odot}$ over 10^9 yr would probably be regarded as a reasonable upper limit. The largest enhancement factor of 40 presented here, which reduces the observed rate to about 250 $M_{\odot}$ yr^{-1}, is thus too small by about an order of magnitude. Exact general relativistic calculations of the effect will probably reveal that the figure of 40 is an underestimate. But perhaps the most promising avenue for further research is the possibility of combining this effect with another one, such as that described by Misner.

Lawrence[11] has proposed a related model, and invokes flattened rotating objects (spinars) to produce the enhancement. But I believe his treatment to be inadequate, and in any case there are significant qualitative differences between his effect and the one described here. In particular, a thin disk, and the associated "multiple crossing" phenomenon described above, are essential for this effect.

I thank Professor Martin Rees for pointing out an error in an earlier version of this paper, and for subsequent valuable conversations. I thank the referee for bringing the work of Lawrence to my attention.

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Measurements of Some Hydrogen-Oxygen-Nitrogen Compounds in the Stratosphere from Concorde 002

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Measurements of the sub-millimetre wavelength far infrared emission spectrum of the stratosphere were made from Concorde 002 during the tour of the Far East in June 1972. The spectra have been analysed to provide concentration data for the species H_2O, O_3, HNO_3, N_2O, and NO_2.

PREVIOUS high resolution measurements[1–3] of the sub-millimetre infrared emission spectrum of the stratosphere have shown that, in addition to lines of H_2O, O_2 and O_3, other lines may be observed which are due to species such as HNO_3, NO_2, N_2O and SO_2, particularly at large air masses. The importance of such observations is clearly very great in view of the present scientific debate on the physics and chemistry of the stratosphere, and the possible effects of high-flying aircraft. The work reported here is the first of a series of measurements to determine the concentrations of several of the species of interest, from the far infrared spectrum.

The basic technique[1,2,4] is to use a Michelson interferometer together with a helium-cooled Rollin bolometer, the whole system having a spectral response in the 300 µm to 3,000 µm range. The advantages of this system over others when making atmospheric observations have been previously identified[1,2,4,5].

Apparatus and Data Collection

The apparatus was a modified version of that flown in a Comet 2 previously[1,2], and was installed in Concorde 002 in April 1972. Particular modifications which had to be made included: the manufacture of a special polypropylene window to be fitted into the fuselage in one of the passenger window apertures; the design and construction of a new data logging and control system, for faster scanning of the interferometer than had been used previously; and change of the zenith angle to 90°, in order to increase the air mass viewed by the apparatus. The use of a Cassegrain telescope was abandoned in favour of a radiation collecting horn, with a 5° (total) field of view.

Data were recorded on paper tape and stored for processing. The resolution of the interferometer was 0.067 cm^{-1} (unapodized[6]) and a single interferogram was recorded in 11 min. The equipment, once started, operated automatically, with the scanning motion of the interferometer mirror being reversed by micro-switches.

During the Far East tour, interferograms were recorded wherever possible subject to the following two criteria: first, that the aircraft was flying at sufficiently high altitude to yield stratospheric data; and second, that liquid helium was available. Supplies of liquid helium were arranged through associate companies of the British Oxygen Company Ltd, and with Air Products Ltd. Some fifty-five interferograms were recorded of which thirty were finally used to provide data: the others were rejected because of unsuitable atmospheric conditions, excessive aircraft manoeuvring or because of serious noise interference.

The tour went through Iran, to India, Singapore and Japan; then on to Australia (most of the time being spent in S Australia), and returning *via* Singapore, India and Saudi Arabia. It started on June 2, and the last set of observations was made on June 28 (Table 1). Some data for the UK were recorded before the tour, on shakedown flights.

Sample Spectrum

In Fig. 1 I show a sample spectrum (20/6.3+4 in Table 1) which is the average of two 11 min runs recorded over the Sydney (Australia) area on June 20, 1972. The spectrum has been labelled with assignment numbers, and a partial list of assignments is given in Table 2 for the species HNO_3, N_2O, NO, NO_2 and SO_2. The complete list including H_2O, O_2 and O_3 may be found elsewhere[7]. The lines of HNO_3 and NO_x which have been used for concentration determination are marked in Fig. 1 by an asterisk (Table 2).

Table 1 Volume Mixing Ratios (Assumed Constant with Height)

Run identifier	$VHNO_3$ $X10^9$	VH_2O $X10^6$	VN_2O $X10^9$	VO_3 $X10^6$	Flight h (1,000 foot)	Altitude (mbar)	Tropopause h_t (1,000 foot)	Altitude (mbar)	h–h_t (1,000 foot)	Approximate latitude and longitude	
30/5.1	2.0	3.93	240	4.9	48	140	38	230	10	48N	08W
9/6.2+3	3.1	5.50	300	4.6	50	120	52	105	−2	01N	104E
11/6.1+2	3.4	6.60	275	4.6	48	125	50	115	−2	05N	110E
11/6.3+4	2.8	6.22	270	4.8	51.5	110	50	115	1.5	10N	115E
14/6.1+2	3.2	6.55	325	4.6	47	145	52 to 55	85 to 105	−5 to −8	35N	140E
15/6.2	2.9	5.70	270	5.5	44.5	155	52.5	100	−8	30N	135E
15/6.5	2.7	6.80	365	5.1	48	130	53	95	−5	18N	121E
20/6.1+2	3.7	5.90	265	4.8	45	150	37.5	230	7.5	35S	151E
20/6.3+4	3.0	3.60	190	3.7	49	120	37.5	230	11.5	35S	151E
20/6.6+7	1.9	2.85	215	4.8	47.5	130	37	235	10.5	37S	149E
20/6.8	2.7	3.60	215	3.7	40	195	37	235	3	40S	145E
22/6.2	2.1	3.15	210	4.9	49	125	39.5	200	9.5	40S	145E
22/6.3	3.0	5.62	350	5.4	40	195	39.5	200	0.5	40S	145E
23/6.1+2	2.5	2.49	240	4.0	52	105	37	235	15	30S	140E
23/6.3+8	2.7	10.2	390	5.9	40	190	52.5	100	−12.5	20S	133E
23/6.12+13	2.5	9.21	250	3.9	47	145	54	90	−7	12S	125E
23/6.14+15	3.2	8.75	245	4.9	52	105	52.5	100	−0.5	05S	115E
24/6.3	1.9	12.9	270	3.7	44	155	*	—	—	01N	104E
28/6.1+2	3.5	16.1	250	3.4	35	260	52.5	100	−17.5	20N	70E

* No meteorological data available.

The spectrum was assigned, using the compiled data[7], and the equivalent widths of the lines of interest were measured manually and tabulated. For H_2O and O_3 a technique[4,8] of deriving the mixing ratio relative to O_2 emission lines was used. For the other species, which are in the weak region of the curve of growth and so cannot simply be compared with strong O_2 emission lines, laboratory measurements[9–12] and calculations[13,14] have been used to calculate the equivalent path length of the species above the aircraft. A correction for the temperature of the stratosphere (assumed to be 225 K) was made, and the equivalent path expressed in units of cm atmos. The data were then treated in two ways. First, the concentrations were converted to units of column density, cm^{-2} (that is, the number of molecules above the flight level in a column of 1 cm^2 cross-section). Second, it was assumed that the mixing ratio was constant with height, and a standard curved atmosphere model[15,16] was used to derive the total air mass (in cm atmos) with which to produce the volume mixing ratio, V, for each species. This is, of course, certainly not true for several of the species: however, vertical distributions of mixing ratio were not the prime concern of this work, and will be considered later. This mixing ratio therefore is an effective mean value (averaged over height) for each species. For the gases emitting in the weak region of the curve of growth (HNO_3, NO_x, weak O_3) the scale height is the atmospheric scale height. For H_2O and strong O_3 lines the scale height is smaller (~2 km in the vertical for H_2O). Both column density and average mixing ratio are listed in Table 3.

Global Data

Individual values of volume mixing ratios then derived in this way for H_2O, HNO_3, N_2O, and O_3, are given in Table 1, where I also give details of the flight level, tropopause level, and approximate geographical location. An estimate for the total amount of NO_2 has also been made[6], but the spectral assignments are somewhat uncertain for this species (see below), and so no results have been given in Table 1.

In Table 3 I give the global averages for the data, with an estimate for the spread in values obtained. The errors involved in this spread will include random errors in equivalent width measurement (including the effect of noise in the spectrum), fluctuations in air mass due to aircraft roll and manoeuvring, and real variations due to height, h, tropopause height h_t, or latitude change. The data also include a contribution due to systematic errors in source spectroscopic data[9–14], which have been considered elsewhere[7]. The systematic errors are due to poor signal-to-noise ratios in the laboratory spectra, incorrect transmission coefficient estimates, and lack of theoretical data on line strengths and half widths.

Total Concentrations and Mixing Ratios

For my present purposes I wish to report only on measured total concentrations and mean mixing-ratios, as the first stage in this programme of work. But I note that in several cases, the behaviour of volume mixing ratio as a function of height indicates variations which are possibly significant. Fig. 2 shows examples, for H_2O, N_2O and HNO_3, of data taken from Table 1. The lines have been hand-drawn through the points. These trends are being considered and I hope that vertical distribution profiles will be evaluated, together with further measurements at several zenith angles.

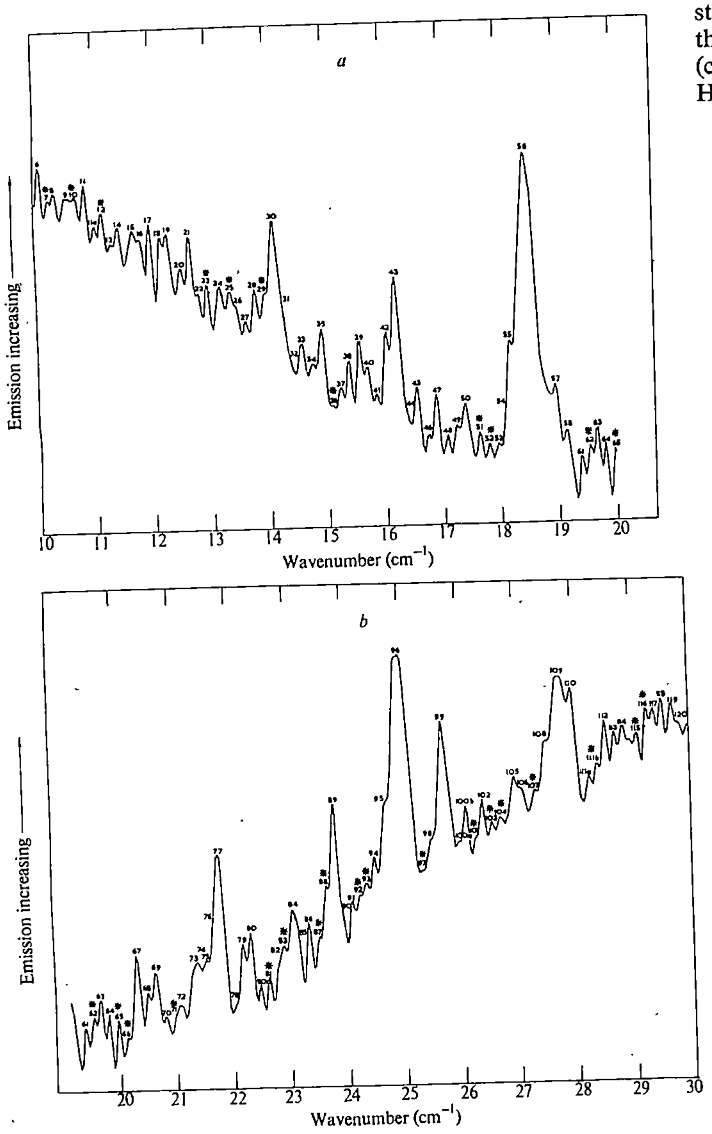

Fig. 1 The average of two spectra at a resolution of 0.067 cm^{-1}. The numbers refer to the full assignment table to be found in ref. 7: a partial list is given in Table 2 for the asterisked lines, which are those due to HNO_3, N_2O, NO_2 and SO_2. *a*, 10–20 cm^{-1}; *b*, 20–30 cm^{-1}.

I now summarize the results obtained to date, with a brief species-by-species discussion, and compare these with measurements and calculations by other workers.

For HNO_3, values fairly closely grouped around a mean mixing ratio of 3×10^{-9} are obtained. No significant latitudinal variation is observed (Table 1), but some evidence of a non-linear vertical distribution may be derived from the behaviour with height above the tropopause (Fig. 2). HNO_3 has previously been observed by Murcray *et al.*[16], and Rhine *et al.*[17] have interpreted their results to be equal to an average mixing ratio of about $3.2\pm30\%\times10^{-9}$, with an "ozone-like" distribution. Lazrus *et al.*[30] obtain lvaues between 2 and 4×10^{-9} at 20 km. Recently Murcray (private communication) has obtained values of 4.5×10^{-9} by volume at about 23 km, with about 1×10^{-9} at 15 km.

N_2O has been measured in the troposphere and the stratosphere by a number of workers, because of its importance in the nitrogen cycle. Schutz *et al.*[19] obtain very similar results to those of Table 3, of 250×10^{-9} at the tropopause and 220×10^{-9} at about 15 km. Goldman *et al.*[20] obtain a distribution of similar shape, but with lower absolute values, reporting 150×10^{-9} at the tropopause. Bates and Hays[21] have considered the factors affecting the concentration of N_2O in the stratosphere, and present a number of profiles depending on the adopted value of the vertical exchange coefficient K_z (cm^2 s^{-1}). My results indicate, using Fig. 3 of Bates and Hays, a best fit with K_z equal to 1×10^3 cm^2 s^{-1}.

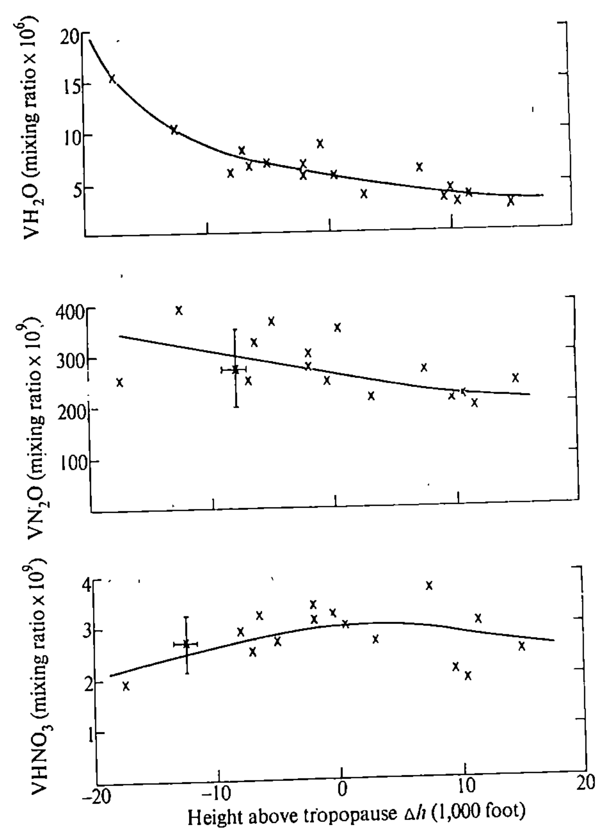

Fig. 2 A compound diagram showing the variation of VH_2O, VN_2O and $VHNO_3$ with height above the tropopause. The curves are hand drawn through the data points and the significance of the variations is discussed in the text.

In the case of NO_2 my results give about 20×10^{-9} by volume. As mentioned above, however, the accuracy of this measurement is severely limited as the spectral assignments are somewhat uncertain (lines 71 and 83 in Table 2) and, in addition, source spectroscopic data are of poor quality. More work is currently being done on NO_2, and it is hoped that we will be able to make a more definite statement regarding this species soon. The only other estimate is one by Ackerman and Muller[23], who have used data obtained by Murcray and co-workers, from a balloon at 32 km, as well as their own data, to produce a profile of NO_2 which varies between 10^{-9} and a maximum of about 10×10^{-9} centred at about 28 km. This estimate is considerably lower than mine. But until the accuracy of source spectroscopic data has been established in both the spectral bands it is probably more meaningful to comment on the similarity of the results. The

Table 2 Partial List of Assignments

Line number	Measured wavenumber (cm^{-1})	Predicted wavenumber (cm^{-1})	Species
7	10.181	10.25	HNO_3
10	10.650	10.65	HNO_3
		10.72	N_2O
12	11.064	11.08	HNO_3
23	12.963	12.96	HNO_3
25	13.200	13.14	HNO_3
29	14.10 (sh)	13.94	HNO_3
36	15.094	15.06	N_2O
51	17.593	17.58	N_2O
52	17.70	17.75	HNO_3
62	19.566	19.566	SO_2
65	19.988	20.09	N_2O
66	20.172	20.26	NO_2
		20.26	HNO_3
71	20.944	21.01	NO_2
81	22.578	22.59	N_2O
		22.62	HNO_3
83	22.96 (sh)	22.89	NO_2
87	23.59 (sh)	23.45	N_2O
88	23.71 (sh)	23.67	HNO_3
92	24.262	24.18	NO_2
		24.26	N_2O
93	24.375	24.45	HNO_3
97	25.381	25.45	NO_2
		25.48	SO_2
101	26.287	26.14	HNO_3
103	26.609	26.54	HNO_3
104	26.766	26.73	NO_2
		26.76	N_2O
107	27.325	27.39	HNO_3
		27.339	O_3 (weak)
111b	28.47	28.44	NO
		28.50	SO_2
115	29.119	29.05	HNO_3
116	29.280	29.28	N_2O
		29.29	NO_2

sh=Shoulder; full list of assignments given in ref. 7.

column density of NO_2 which I have calculated approximately from Ackerman and Muller's data is 6.5×10^{15} cm^{-2}, to be compared with my result of about 5×10^{16} cm^{-2}. The latter figure will be revised in the near future once improved source data is available.

Table 3 Global Average Stratospheric Mixing Ratios

Species	Column density (mol cm^{-2})	Average volume mixing ratio	Comments
H_2O	7.7×10^{18}	$(3.0\pm0.3)\times10^{-6}$	Rapid increase below tropopause. Constant up to 60 km
O_3	1.2×10^{19}	$(4.8\pm1.0)\times10^{-6}$	Naturally variable
HNO_3	7.2×10^{15}	$(2.8\pm0.7)\times10^{-9}$	
N_2O	5.4×10^{17}	$(210\pm50)\times10^{-9}$	Measured 3 km above tropopause
	7.0×10^{17}	$(270\pm60)\times10^{-9}$	Measured at the tropopause

For water vapour our group has made a large number of observations over several years[4,5,29] which agree well with the present result of 3×10^{-6} by volume in the stratosphere, constant with height up to about 60 km[29]. Houghton *et al.*[24] have obtained results around 5×10^{-6}, and Mastenbrook[25] quotes values of 3–4×10^{-6}. Our estimates for H_2O should be accurate to better than ±10% (refs. 4, 5). Shimazaki and Laird[26] calculate that at about 70 km the mixing ratio is about 3×10^{-6}, and decreases at higher altitudes.

The result I obtain for ozone is, as for the other species, averaged over altitude, tropopause height and location, and so is an average value which does not reflect any of the known seasonal trends. It would, for instance, have been interesting to observe at more southerly latitudes than 40 S in order to attempt to detect any polar increase. But the average value I obtain is in good agreement with known values[27].

Because the O_3 amount is known to vary considerably with time and location, and because some of the species of interest are thought to be associated with O_3 (for example, HNO_3, NO_2), it is at least possible that these species will exhibit similar fluctuations. In this sense, again, any real variations will tend to be lost in the imposed variations of height, latitude, and tropopause height necessary during this experiment (Table 1).

Finally, though I have not quoted a result in Tables 1 and 3, I mention a first estimate which has been made for the mixing ratio of SO_2: this result, which is based on the tentative assignment of line 62 to SO_2, is approximate, and confirmation will have to await more accurate source data and better experimental resolution. But at present I obtain an upper limit of 3.5×10^{-9} for VSO_2.

Many people have been involved in these experiments. I list significant group leaders. At the NPL, Mr N. R. Swann designed and built the control electronics, and assisted in the experiment. Dr N. W. B. Stone also helped.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Rotation of the Earth from AD 1663–1972 and the Constancy of G

TIMINGS of 40,000 lunar occultations of stars from 1943–1972 have recently been analysed to determine improvements to the Moon's orbital elements, and difference between the ephemeris (ET), universal (UT) and atomic (IAT) time scales. Full details are to be published elsewhere, but the analysis for the period for which the atomic time scale is available are of immediate interest. They can be used in conjunction with results of earlier analyses to give a clearer picture of variations of the rate of rotation of the Earth and to provide evidence that is relevant to whether the constant of gravitation, G, is variable.

For 1955.5 to the present, the variations in the rate of rotation of the Earth are given by the difference between UT and IAT. The observed times of occultations of stars by the Moon were therefore expressed on the scale IAT+34.24 s (an approximation to the particular ephemeris time scale, ET2, which is the time argument of the currently-adopted lunar ephemeris[1]) and used in a least squares analysis to determine corrections to the orbital elements on which the current lunar ephemeris is based. The resulting correction to the expression for the mean longitude of the Moon is (in arc s)

$$\Delta L = -(0.08 \pm 0.02) + (1.4 \pm 0.1)(T - 0.63) - (10 \pm 3)(T - 0.63)^2 \quad (1)$$

where T is the time in centuries from 1900. We can interpret this as arising from the difference between ET2 and (IAT +32.24 s); thus since the mean longitude of the Moon increases by 1 arc s in 1.821 s

$$\mathrm{ET2} = \mathrm{IAT} + (32.39 \pm 0.04) - (2.55 \pm 0.18)(T - 0.63) + (18.21 \pm 5.46)(T - 0.63)^2 \quad (2)$$

This implies that, at 1963.0, IAT+32.39 s would be a better approximation to ET2 and that the second of the ET2 scale is equal to $(1.0 - 0.8 \times 10^{-9})$ SI seconds, or (9, 192, 631, 762 ± 1) cycles of the defining caesium transition. The quadratic term could be interpreted as arising from a fundamental linear increase of the duration of the ephemeris second implied by gravitation theory with respect to the SI second, but it is more reasonable to attribute it to an error in the earlier correction [see equation (3)] applied to the lunar theory of Brown[2] to reduce the time argument to agree with ephemeris time defined by Newcomb's[3] theory for the Sun. The time scale obtained by applying this further correction to the mean longitude is here denoted by ET*: it is a dynamic time scale that corresponds as closely as possible to the atomic time scale over the common period.

The previously tabulated values of $\Delta T = \mathrm{ET2} - \mathrm{UT}$ should be corrected by the value of ET2−(IAT+32.24) from equation (2) in order to give a better representation of the variations in the rate of rotation of the Earth. Applying this correction to the annual mean values given by Martin[4] for 1663–1860, by Brouwer[5] for 1861–1949 and in the Astronomical Ephemeris[6] for 1950–1972, we obtain the differences, $\Delta T^* = \mathrm{ET}^* - \mathrm{UT}$, shown in Fig. 1$A$. The accumulated time difference, ΔT^* s is caused by variations in the length of the day with respect to the length of the mean solar day near 1900.

The curve in Fig. 1A is of a parabolic form (corresponding to a gradual increase in the length of the day, due to tidal friction), but it is better represented by three parabolic arcs of steady deceleration of the rate of rotation of the Earth, linked by shorter periods of rapid acceleration, together with fluctuations about these mean rates. Representative values of the excess of the length of the day in ms with respect to the day near 1900 are given by the first derivatives along the dashed curve in Fig. 1A and are shown in B.

I have looked for, but have been unable to find, any differences in the interpretations or methods of analyses of the data which could have led to the major departures from a constant rate of deceleration as shown in Fig. 1. It is therefore necessary to find some cause (such as differential motion at the core-mantle interface[7,8]) to account for the large fluctuations.

The adopted coefficient (+7.14″) of T^2 in the theory of the Moon's motion due to Brown is a theoretical value that takes into account the gravitational and precessional effects, but

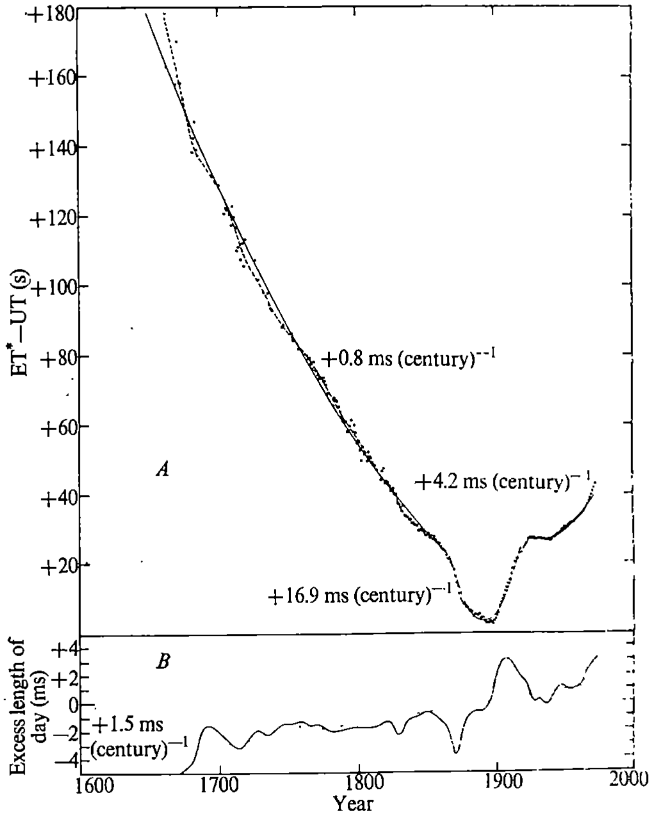

Fig. 1 A, Accumulated time difference on an adjusted ephemeris time scale, ET*, due to variations in the length of the day relative to the reference day near 1900. The three solid curves correspond to constant rates of increase in the length of the day. B, Excess length of the day compared with the day near 1900. The curve is the first derivative of A. The dashed line is the average rate of increase of the length of the day.

does not make any allowance for tidal interactions in the Earth–Moon system. The lunar ephemeris is now based on the value $-4.08\ T^2$ which follows from the addition (first proposed by Clemence[9]) of the correction

$$\Delta L = -8.72 - 26.74\ T - 11.22\ T^2 \qquad (3)$$

which was deduced from analyses by Spencer Jones[10] of observations of the Sun, Moon and planets from 1700–1930. Thus, combining equations (3) and (1), we obtain a term $(-21'' \pm 3'')\ T^2$ for the observed additional (tidal) deceleration of the Moon in mean longitude with respect to atomic time from 1955.5–1972.0. This supports the result of Van Flandern[11] of $(-26 \pm 8)\ T^2$ from occultations, and is in good agreement with the value of $(-19 \pm 4)\ T^2$ obtained by Oesterwinter and Cohen[12] who analysed meridian observations of the Sun, Moon and planets for the period 1912–1968. It also agrees with a value of about $(-19 \pm 3)\ T^2$ deduced from ancient solar eclipses[13,14] with a mean epoch around AD 0.

Assuming transfer of angular momentum in the Earth–Moon system and adding a part for the Sun's tidal torque, a value of $-20\ T^2$ corresponds to a rate of change of $+4$ ms $(\text{century})^{-1}$ in the length of the day. On the other hand, the value of ΔT ($\sim +4.5$ h) determined from the eclipse data gives an average rate of only $+2$ ms $(\text{century})^{-1}$. The average rate for the period 1663–1972 from Fig. 1 is $+1.5$ ms $(\text{century})^{-1}$.

Thus we are faced with two difficulties. First, why does Spencer Jones's result of $-11\,T^2$ differ so much from the other results? Second, what causes the implied average non-tidal rate of change of -2 ms $(\text{century})^{-1}$ in the length of the day?

Spencer Jones's result is strongly dependent on the analysis of times of transit of Mercury across the Sun, and Williams[15] and Clemence[16] have confirmed his values. A possible explanation of the first problem is that Mercury has a deceleration of $(-3.1 \pm 0.9)\ T^2$ in mean longitude which does not arise from the gravitational theory of its motion.

Hoyle[17], in his recent presidential address to the Royal Astronomical Society, however, has suggested that both anomalies can be resolved if the constant of gravitation, G, varies inversely with time, provided that the value of the Moon's deceleration from ancient eclipses is interpreted as including both tidal and non-tidal (that is, depending on $\dot{G}$) components. There is little doubt that my value obtained directly with reference to IAT does so; but there is doubt about that from the ancient eclipses. It seems to me that the value of the deceleration obtained from ancient eclipses is measured with respect to a gravitational time scale, and that any variation of G with respect to an atomic time scale will not be apparent. If this argument is valid, the deduced value includes only the tidal component. It follows that the close agreement of this value with that deduced with respect to IAT suggests that $G = 0$, or, allowing for an uncertainty of $\pm 3\ T^2$, $\dot{G}/G \lesssim 2 \times 10^{-11}$ yr^{-1}. (The relationship between the units in Hoyle's paper and those above are as follows. If d is the rate of change in the length of the day in ms $(\text{century})^{-1}$, $\dot{\omega}/\omega = -0.12\ d\ \text{aeon}^{-1}$, where an aeon is 10^9 yr: $\dot{n}$ is twice the coefficient of T^2.) An extension of the work of Spencer Jones to include observations since 1937 is urgently required.

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The Orbit of Halley's Comet

RECENT investigations by Brady[1] have yielded the suggestion that the historical observations of Halley's Comet can be interpreted as indicating the existence of a large planet beyond Pluto having an orbital period of 464 yr. One of us[2] has carried out a detailed study of the past orbit of Halley's Comet using an extension of Cowell and Crommelin's method of Variation of Elements. Either Kiang's material[2] was capable of showing Brady's result but it had not been noticed; or his calculations were insufficiently accurate; or Brady's result was better accounted for by another explanation. We have attempted further calculations to decide between these alternatives, and we now believe that the third alternative is correct.

Brady first found that, by comparison with the observed times of perihelion passage, the theoretical motion of a body following the orbit of Halley's Comet was much improved, after full allowance was made for the gravitational effects of the planets, by incorporating a small empirical term in the equations of motion: explicitly this term was in the nature of a secular change in the central mass (the Sun). But from the kinematic point of view, an almost exact equivalent would arise from successive tangential impulses to the motion which might, as far as could be told from the observations, occur at or near the time of perihelion passage. Kiang's average "non-gravitational" change of mean motion over successive returns had been thought to be caused by a recurrent tangential impulse near perihelion passage arising from the interaction between reaction from solar heating and rotation of the comet nucleus. Such non-gravitational effects were the basis of evidence originally put forward by Whipple[3] in support of his ice-rock agglomerate model of comets. Further, the size of Brady's empirical term is just that which would account for the average change in mean motion per revolution previously calculated, and if the minor modifications in recorded perihelion-passage times, which had been evaluated as an intrinsic part of Kiang's investigation, are incorporated into Brady's orbital comparisons where he used his empirical term, the already small residuals found by him would be further reduced, rather markedly. Without the benefit of this extra encouragement, however, Brady was not wholly satisfied with his empirical term and he therefore sought an explanation from gravitational effects of an unknown "Planet X", especially when he found that the residuals in perihelion passage behaved in a quasi-sinusoidal way with a period of about 600 yr if the empirical term were omitted.

We therefore turned our attention to the question of how a long periodicity could arise in the departures from a theoretical orbit through the effect, say, of a tangential impulse occurring once per revolution of the comet in its orbit, that is, every 76 yr. That such an apparent periodicity is possibly an inherent tendency is indicated by Fig. 1 of ref. 1 which shows the effect on the expected time of perihelion passage due to neglect of the gravitational attraction of Pluto. This, with a small amplitude, shows a quasi-period of about 600 yr, even though Pluto's period is 248 yr.

We considered a simplified numerical model consisting of the Sun, Jupiter and Halley's Comet. Full details will be published later; in brief, we found that Brady's quantity ΔT (departure from predicted time for a particular orbital position) can be represented as governed by a linear second-order differential equation in which the coefficients are periodic with the periods and beat periods of Jupiter and Halley's Comet. There is a formal resemblance between this equation and Hill's equation[4] in lunar theory and we expect that it will be possible to show from the analysis how a dominant long-period term can emerge. Numerical solutions of the equation have been found to show a long-period variation (600–700 yr) for a range of initial conditions. We believe that any error, whatever periodicity it may have, will propagate with a long periodicity, the exact value of which is an intrinsic property of the 3-body configuration.

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The Geophysical Consequences of Professor Lyttleton

HAD Professor Lyttleton sent me his letter[1] before publication, I would have suggested that he replaced his homely parable with a straightforward account of how his controversy with me has—unhappily—arisen. To judge from his recent review[2], from which the quotations I will use are drawn, he has become seriously displeased that his attempts to revive Ramsey's theory[3], that the Earth's core is not iron but a phase change undergone by ferromagnesian silicates of the mantle at high pressure, has not "for some curious reason . . . found much favour with geophysicists". He extended Ramsey's theory by postulating that the pressure at which this hypothetical phase change occurs decreases with increasing temperature. Thus starting with a cold accreted Earth—wholly of silicate with no iron core—the disseminated radioactivity heated the Earth up to the temperature at which the phase change to a denser state began at the centre. Thus the core grew and the Earth's radius contracted.

Using an empirical relation between bulk modulus and pressure for the Earth's mantle and core at the present time, which seismology provides, along with the laws of gravitation and mechanical equilibrium, Professor Lyttleton produced a host of models of the density distribution and constitution of the evolving Earth with various sizes of the growing core and of the Moon and each terrestrial planet[2]. For the parameters of these models[2] he claims "considerable numerical precision". I note, in passing, that the empirical relationship at the basis of his computations is not a true equation of state as it does not include temperature.

His conclusion that the Earth's radius has decreased by about 300–400 km during its life, which he announced as a theory of mountain building[4] (the classical theory of the shrinkage of the Earth's crust by the supposed cooling of the interior had been judged quantitatively inadequate), unfortunately appeared just as geologists and geophysicists had come to take seriously the great variety of new evidence for continental drift[5]. The contractions of the crust in mountain building began to appear as a second order effect compared with the great displacement of the continental blocks, rather than as the fundamental problem of tectonics.

Professor Lyttleton[2], much concerned, sought to warn geophysicists against "their transport of enthusiasm for the postulates of convective and other motions that are the main concern of geophysics today", and helpfully tried to steer them away from unproductive researches: "For what becomes of the theory so created (of those postulated motions, such as continental drift) if the phenomenon itself fails to materialize?" and alerted them to the possibility that the whole question might lead to a *reductio ad absurdum*: "are all the continents moving, or are some fixed on the Earth and some moving . . . What happens when all the continents come together again?—the surface of the sphere has a limited area—do they do so simultaneously and after fitting together almost perfectly bounce back again, or do they slide over each other?" Perhaps lessons drawn from the progress of other sciences, of which geophysicists were doubtless ignorant, would help: "the past half century has seen enormous strides in the theory of stellar structure that have depended as far as the surface is concerned on ignoring practically everything . . . the procession of surface events associated with the sunspots, fascinatingly intriguing as these are, do not find any place in the theory".

Nevertheless, Professor Lyttleton[2] recognized "that at present there is a large number of geophysicists who are inclined strongly to the view that continental drift is occurring, just as there are probably many people still that are inclined to the view that flying saucers visit this planet". How to convince them that "these conclusions are based on entirely inadequate evidence" other than by using the same "arguments of a verbal kind" which he was condemning? Obviously what was needed was quantitative refutation of key parts of the theory!

The paper[6] of mine, to which he refers, is largely concerned with arguing that continental drift is brought about by thermal convection in the solid mantle, made possible by a solid state creep process. The analysis of satellite orbits had revealed the presence of non-hydrostatic, low harmonics of the geoid, confirming earlier work by Jeffreys, but geodesists had attributed them to the classical view of a rigid mantle in which density anomalies had arisen, accidentally, in the early history of the Earth. I argued that this important discovery could be better explained by the density differences driving the convection currents in the mantle, and that therefore the data contained information about the pattern of laminar flow in the mantle. Until recently, geodesists ignored this theory, presumably hoping it would go away, but Professor Lyttleton[2] took a firmer line: "the departure from hydrostatic equilibrium was said to be due to the currents themselves. Clearly, however, there is no possibility of currents as small as 1 centimetre per year producing non-equilibrium elevations of the free surface of the Earth of the order of 0.1 km. The energies per unit mass involved in the currents is negligible, and it would require speeds of many metres per second to achieve any appropriate surface elevation even were some suitable mechanism available." But Bernouilli's equation, appropriate in determining the height to which a fountain will play, cannot be applied to the mantle[7], for, as I had shown[8], the viscous term in the Navier–Stokes equation of flow in the Earth's mantle is about 10^{20} greater than the inertia and acceleration terms. In fact the distortion of the gravitational equipotential surface due to convection equals the viscous (or buoyancy driving) force per unit volume (10^{-2} dyne cm^{-3}) multiplied by the cell size (10^{8}–10^{9} cm) divided by the gravitational acceleration and density, and is of the right order of magnitude.

The second criticism which he made of my paper[6], and which he now renews in his letter[1], concerns its most speculative part. I had suggested that the break-up of the protocontinents and the present directions of movement of the continents arose from a change in the convection pattern in the Earth's mantle about 100–200 m.y. ago. I pointed to the clustering of the ages of rocks in the shield areas all over the world around three dates in the Precambrian as evidence that earlier changes in the convection pattern and earlier upheavals of the continents had taken place—a speculative idea, though recently receiving considerable support from palaeomagnetic surveys of Precambrian rocks[9]. I finally suggested that such successive changes in the convection pattern might arise from the changing geometry of the convecting mantle by the gradual settling of iron towards the centre, suggested originally by Urey[10]. To illustrate the possibility that this hypothesis of a growing core might be tested by measurements of the supposed daily, monthly and annual growth increments in certain Phanerozoic fossils[11], I calculated the changes in the moment of inertia (and in the gravitational energy) as the core grew during the Earth's life. For the case of an iron core, these changes are the first order effects of a growing core, while the changes in the overall radius of the Earth are a second order effect, as can easily be seen by a rough calculation; thus in my work I took the radius of the Earth to be (nearly) constant. This Professor Lyttleton criticized as "manifestly invalid", claiming to have solved the problem exactly, in a paper which he submitted to the Royal Astronomical Society "On Possible Causes of Change in the Volume of the Earth" and read at the meeting of the society on January 9, 1970. The report of this meeting[12] and the paper were not seen by me until September of that year when the society decided to publish it. I then wrote a letter to *Observatory*[13], and a paper to follow his in the *Geophysical Journal* of the society, explaining that I had made an entirely legitimate approximation ("which is a discernment that certain factors and complications do not contribute appreciably . . . a faculty to be cultivated, not a vicious propensity"—Eddington quoted by Lyttleton[2]). I also corrected an error in the ordinate scale of Fig. 11 (b), which should read $0-1.8\times10^{38}$ erg, not $0-18\times10^{38}$ erg. I should perhaps in my original paper have specifically said that the calculated quantities—moment of inertia and gravitational energy—of the models were accurate to about one per cent.

Professor Lyttleton's solution, using the mathematical methods already described with which he was well satisfied ("such questions require formal analysis for their safe treatment"), is given in *Observatory*[12] and in his review[2], and was developed fully in the paper already referred to. It is that, if the Earth had been a uniform mixture of iron and silicate at its origin and the iron had settled to form the core, its total gravitational potential energy (W) would have changed from 0.2263 to 0.2521×10^{40} erg and its moment of inertia factor (f) from 0.3789 to 0.3187, the radius of the Earth decreasing by 43.0 km. This latter he described as "of great geophysical importance"[2] and commented "Whether this is enough for all mountain building is a geological question, but, if not, there remains the phase-change hypothesis". I had to point out, however, that nowhere in Professor Lyttleton's discussion was the heating of the earth by the release of about 2.6×10^{38} erg of gravitational potential energy taken into account[13]. The Earth heats up and expands, the latter process absorbing perhaps a quarter to a third of this energy. As its volume is about 10^{27} cm^3 and the thermal capacity of silicates at NTP about 0.6 cal cm^{-3} °C^{-1}, its internal temperature would rise by between 2,000° C and 3,000° C, if no heat escaped (allowing for a possible increase by a factor of two to three in the thermal capacity towards the geocentre). The linear coefficient of thermal expansion is about 10^{-5} °C^{-1} in the laboratory, giving an increase in the Earth's radius of 2–3%, 120 km–180 km, more than annulling Lyttleton's effect, even if the poorly known decrease of the coefficient with depth is as much as a factor of five at the geocentre (three is usually given). The values for the moment of inertia and the gravitational energy change by a similar proportion. After I had corrected the proof of my paper, the Royal Astronomical Society informed me that Professor Lyttleton had withdrawn his paper.

I now return to the incompleteness of the equation of state he uses. In the Earth and Venus the change in density with depth due to pressure greatly outweighs that due to temperature. For example, in the Earth's mantle, the density changes from 3.3 at the surface to 5.6 at the core-mantle interface, but the most the density decreases due to temperature is only 0.3. The neglect of temperature is not too serious for many purposes except for precise calculations and the determination of second order effects. In the Moon and Mars, however, the changes of density due to pressure and temperature are comparable, and as their thermal state is almost entirely unknown Lyttleton's conclusions[2] concerning the non-existence of small iron cores (that is, of radii some hundreds of km) in these bodies are unsound. Analogies with Eddington's work on the internal constitutions of stars are misleading. The physics of the solid states does not lead to any simple, widely applicable equation of state like the gas laws and the chemistry of planetary interiors is complex. But solid cosmic bodies possess a memory: the key to their evolution and constitution lies in the physico-chemical record preserved at their surfaces.

Professor Lyttleton's present letter[1] alleges that in my reply[13] to him I confused the mathematics and the physics of the problem. But unless one has a definite theory of what happens to the released gravitational energy, it is clear that the problem cannot be specified to the precision he seeks. The lack of this invalidates hundreds of calculated parameters (r_s, f, W), given to four or five significant figures, in the tables of his papers[2,4] if we are discussing accuracies better than about one percent. It is of interest that Urey[10], Birch[14] and Tozer[15] have also tackled, with various assumptions and approximations, the problem of the energy released per unit mass on the formation of the Earth's iron core, and obtained 670 cal g^{-1}, 600 cal g^{-1}, and 560 cal g^{-1} respectively. I obtained 600 cal g^{-1}.

Regarding the boundary conditions of my solution, I set out completely, but clearly too briefly, what I did. The three first order, non-linear, simultaneous differential equations (see para. 2), which relate pressure p, gravitational acceleration g, and density ρ at all points in the Earth, were integrated inwards from the surface where $p=0$ and its radius and g on it taken to be the present values. The surface value of ρ_s is varied between models to represent different mixtures of iron and silicate in the mantle. But consider an entirely general model of a planet, chemically homogeneous, with a known relation between $\rho\ \mathrm{d}p/\mathrm{d}\rho$ and p applying everywhere; it would be found that, following the procedure just described (assuming a fixed external radius and arbitrary, but allowable, values of ρ and g at the surface), g and $\mathrm{d}p/\mathrm{d}r$ would not vanish at the centre: this mathematical planetary model would possess a central point mass except for certain values of ρ and g at the surface. Suppose now a core, of unknown radius r_c, is inserted in the model, with a different but known $\rho-p$ relation; the point mass can be eliminated and r_c uniquely determined by the imposition of the boundary condition that $\mathrm{d}p/\mathrm{d}r=g=0$ at the centre. I do not see how Professor Lyttleton arrives at an "infinity of solutions" for each ρ_s unless the elementary boundary conditions at the core-mantle interface are omitted. It follows that he is incorrect in stating that "clearly the models [I] obtained have different masses to overcome the incorrect assumption of unchanging radius". Any approximation in a calculation does of course carry others with it and this work is no exception. The overall mass ratio between the silicate and iron varies slightly between each model, but mass transfer between the core and mantle is the point of the calculation. The question naturally arises whether there is a more logically satisfying procedure and I will go into this in detail elsewhere, but I think that, such is the nature of the physical problem, an approximation of the order I made will enter either early or late. Professor Lyttleton does not see this. He is also incorrect in stating that I do not explain how the timescale of the evolving core is obtained: this is given on pages 242 and 243 of ref. 6.

As Professor Lyttleton's results from his mathematics on the iron core model in his withdrawn paper still stand in the *Observatory* and his review[2] (Table IX) and on the phase-change core models in his other papers[2,4], might I suggest how a little physics can reinstate them as definitive, exact solutions of the evolving core problem? Clearly the released gravitational potential energy must be removed as the core grows and, as I note that he has not taken up my previous suggested solution[13] of a new cosmological principle, only heat transport remains. Tozer[16], has shown that the hypothesis of thermal convection throws an entirely new light on the vexed question of the thermal history of the Earth, Moon and planets. From the well known result that creep rates depend on a Boltzmann factor, he argues that when the temperature of an initially cold planet reaches a certain critical value, convection then prevents any further appreciable change in the temperature distribution, carrying away all further heat released. But introducing "actual bodily currents into the solid region of the Earth by way of explanation of the observations" seems "premature"[2]. Only conduction remains: but in bodies of planetary size the diffusion of heat by conduction takes place very slowly—typically 100 km in 10^9 y. It therefore follows that the internal temperature distribution of the evolving Earth will remain sensibly constant only if the core forms over (approximately) 10^{13} yr. Provided that this is acceptable, I am ready to admit that Professor Lyttleton has solved the problem of the growing core with satisfying mathematical rigour, superseding my approximate solution, which in spite of being "entirely valueless" seems to have put him on the path to a result of momentous cosmological importance.

Before geochemists rush in to protest that the Earth is only 4.6×10^9 yr old may I suggest that they study Professor Lyttleton's critical appraisal[2] of their scientific method? Their determinations are made on a minute sample of only "one hundredth of one per cent of the whole mass of the Earth . . . and, coming as it must entirely from the present surface layers, even this material may be to some extent peculiar in that it has undergone processes from which the deep interior may probably always have been screened" (two "homely parables" about paint on automobiles and soot on chimney sweeps follow). Let them not therefore add to the "welter of uninformed invalid criticism, that rolls back like the stone of Sisyphus on any theoretician who attempts to bring some order to the rag-bag of raw observations" in which, clearly, radioactive age determinations belong as well as "directions of magnetization of rocks, curious magnetic anomalies on the ocean floor, actual displacements at faultings" geologists' "multitudinous observations in the field", shock-wave velocities in rocks to say nothing of "mere correlations" such as "the close fit of the margin of the African continent into that of South America".

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Mantle Plumes, Palaeomagnetism and Polar Wandering

DUNCAN *et al.*[1] have analysed the igneous activity in the Central Volcanic province of Europe and the Thulean province of Iceland, the Faeroes and the British Isles on the assumption that these provinces represent plume traces. Assuming that plumes are fixed to the mantle and that plume traces are due to lithospheric plate motion only, Duncan *et al.* showed that the motion of the European plate over the past 50 m.y. is not in accord with palaeomagnetic data unless motion of the mantle with respect to the rotation axis (polar wandering) has occurred. Polar wandering of 23° along the 123° meridian was required since the early Tertiary.

Unless some absolute frame of reference, such as fixed mantle plumes, can be found polar wandering is an unnecessary concept in plate tectonics because the only available frame of reference is the Earth's axis of rotation[2,3]. But, McKenzie[2] has shown that the concept of polar wandering could be useful if the rate of relative motion of all plates relative to the pole is very much reduced by a particular choice of polar wandering direction and velocity. In the present discussion it is relevant to consider whether or not there has been any slip of the lithosphere as a whole with respect to the Earth's axis of rotation over the past 50 m.y. This can be done by finding the vector sum of the horizontal displacements of all points on the Earth's surface with respect to the axis of rotation during this interval. An estimate of this net displacement over the past 50 m.y. can be made using palaeomagnetic data for the six major plates of Le Pichon[4].

. McKenzie[2] has shown that the motion of the palaeomagnetic pole P relative to a plate A can always be described by means of an angular velocity vector ${}_A\mathbf{\Omega}_P$ passing through the equator. To allow for the different sizes of plates it is convenient to define another vector ${}_A\mathbf{M}_P$ given by

$${}_A\mathbf{M}_P = f_A \; {}_A\mathbf{\Omega}_P$$

where f_A is the fraction of the Earth's surface area occupied by plate A. The magnitude and direction of polar motion with respect to the whole lithosphere (which can be considered a form of polar wandering) is then given by the resultant angular velocity vector **S**, also passing through the equator, where

$$\mathbf{S} = \sum_{n=1}^{N} {}_n\mathbf{M}_P$$

and N is the number of plates.

The best estimates of the positions of the palaeomagnetic pole with respect to each of the six major plates approximately 50 m.y. ago (early Tertiary) are given in Table 1. The position for the Eurasian plate is the mean of 10 poles derived from the British Tertiary igneous province ($N = 10$, $k = 103$, $A_{95} = 5°$), for the American plate it is the mean of 6 early Tertiary poles derived from cleaning ($N = 6$, $k = 23$, $A_{95} = 14°$), for the African plate it is given by the result from the Ethiopian flood basalts[5] and for the Pacific plate by the data from the California seamounts[6]. The position for the Indian plate is given by the result from the Barrington Volcano in eastern Australia[7], but because there are no results from the lower Tertiary of

Table 1 Magnitude and Direction of Polar Motion with respect to the Six Major Plates over the past 50 m.y.

Plate	Pole (~50 m.y.)	f	Ω (10^{-2} deg Myr^{-1})	M (10^{-2} deg Myr^{-1})	Pole of rotation
Eurasian	75 N, 161 E	0.12	30	3.60	0 N, 71 E
American	85 N, 197 E	0.20	10	2.00	0 N, 107 E
African	81 N, 168 E	0.16	18	2.88	0 N, 78 E
Pacific	71 N, 354 E	0.22	38	8.36	0 N, 264 E
Indian	70 N, 306 E	0.14	40	5.60	0 N, 216 E
Antarctic	80 N, 175 E	0.11	20	2.20	0 N, 85 E

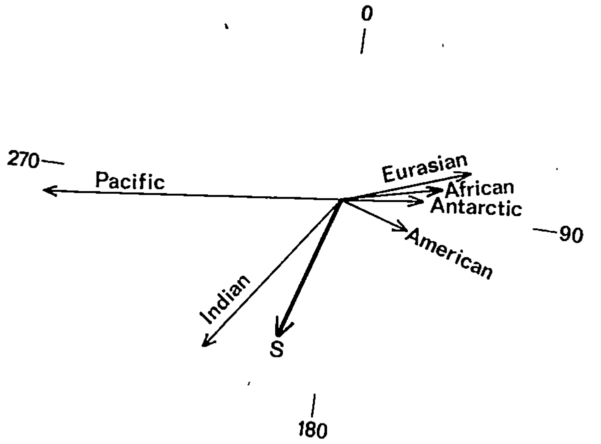

Fig. 1 The vectors **M** describing the polar motion with respect to the six principal plates covering the Earth's surface. The resultant **S** is given by the thicker line. All the vectors lie in the equatorial plane.

Antarctica, the position for the Antarctic plate is found by subtracting the relative motion between Antarctica and Australia (from seafloor spreading) from the Australian Tertiary data[8]. The six principal plates now occupy 95% of the Earth's surface so that the motions of the minor plates may be ignored, although some uncertainty arises from the assumption that the six plates have maintained their present size over the past 50 m.y. In estimating $\mathbf{\Omega}$ for each plate, I assumed that the pole has followed the most direct path along a meridian to its present position.

The magnitudes and poles of rotation of the six vectors ${}_n\mathbf{M}_P$ calculated in Table 1 are illustrated in Fig. 1. The resultant **S** has pole of rotation at 0 N, 198 E and magnitude 2.1° corresponding to motion of the pole with respect to the whole lithosphere of 2.1° along the 108° meridian. This is certainly not significantly different from zero. Even if the poles of rotation for the six plates all coincide, the maximum would be 12.3°. The analysis shows that the conclusions drawn by McElhinny and Wellman[8] about polar wandering since the Eocene are incorrect because they considered only half of the Earth's surface. The integrated effect of motions over the whole surface should be considered. I conclude that there has been no significant motion of the lithosphere as a whole with respect to the Earth's axis of rotation over the past 50 m.y. On the other hand, the calculation of Duncan *et al.*[1] suggests a 23° movement of the mantle with respect to the rotation axis, at least an order of magnitude greater than any lithospheric motion. If I accept the plume calculation I am forced to the surprising conclusion that the lithosphere remains relatively fixed with respect to the rotation axis, but that the mantle inside moves with respect to the same axis. The alternative conclusion is that the underlying assumption made by Duncan *et al.*, that plumes are fixed relative to the mantle, is incorrect.

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Polymers of Improved Modulus by High Pressure Polymerization

Some highly orientated organic fibres[1] are now available with a Young's modulus as high as 130 GN m^{-2}, but most rigid polymers have values between 2 and 4 GN m^{-2}. Even in cross-linked materials, such as phenol formaldehyde resin, it is difficult to achieve values in excess of 7 GN m^{-2}. The reasons for this are to be found in the difficulty in random three dimensional structures of building up a large enough number of bonds per unit volume to have a significant effect upon the properties. It has been suggested (ref. 2 and R. N. Haward, private communication) that cross-linking of organic polymers at high pressures might raise the number of bonds sufficiently to have an appreciable and permanent effect on density, modulus and other physical properties; we have demonstrated that this is so using *p*-divinylbenzene as a model difunctional monomer.

Pure *p*-divinylbenzene[3] in thin walled gold capsules was polymerized by heating to 200–250° C at the desired pressure in a piston-cylinder apparatus[4]. In some experiments *p*-methoxyphenol (100 p.p.m.) was added as inhibitor to ensure that polymerization did not begin before the full polymerization pressure was reached. The density of the product was measured in a density column, the infrared spectrum as a KBr disk and Young's, shear and bulk moduli by an ultrasonic pulse technique[5] at 5 MHz.

Fig. 1 shows the dependence of the density of poly(*p*-divinylbenzene) upon the pressure of polymerization in experiments with inhibited *p*-divinylbenzene. The density of material polymerized at a few atmospheres pressure is about 1.05 (g ml.$^{-1}$ at 23° C) which may be taken to be close to the density of *p*-vinyl polystyrene, which would be expected to be below that of polystyrene ($\sim$1.06). The polymer produced at the highest pressures used in these experiments ($\sim$2 GN m^{-2}) has a

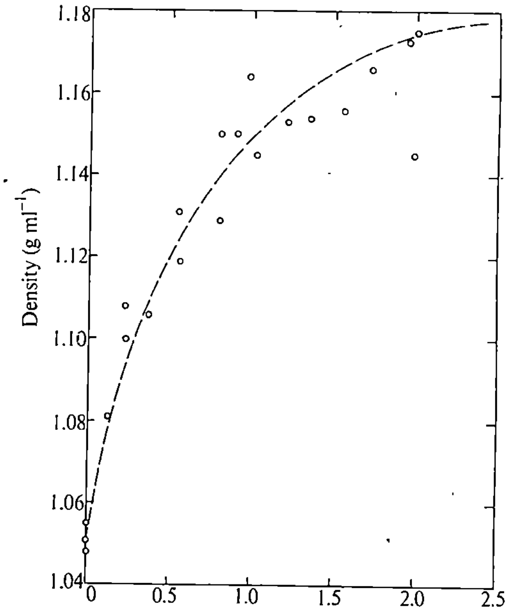

Fig. 1 Variation of density of poly(*p*-divinylbenzene) with pressure of polymerization.

density of ~1.175. It is interesting that styrene containing 20% divinylbenzene gave at 1.25 GN m^{-2} a polymer of density 1.088 gm ml.$^{-1}$ compared with ~1.155 for *p*-divinylbenzene at the same pressure. This demonstrates the effect of reducing the maximum attainable number of cross-links in an otherwise fairly similar system.

Fig. 2 shows the relationship between density and residual vinyl group for all polymerizations. The concentration of residual vinyl groups was estimated from the intensity of the bands at 901 and 837 cm^{-1} in the infrared spectra of the products using the relationship

$$[\text{vinyl groups}] \propto \log_{10}T_a{}^{-1}/\log_{10}T_b{}^{-1}$$

where T is the transmittance at the specified frequency. If it is assumed that polymer of density 1.05 g ml.$^{-1}$ is substantially *p*-vinyl polystyrene then about 36% of the vinyl group still present at this stage—about 18% of that in the monomer—remains as free vinyl group or end group unsaturation in the densest of these materials. Nevertheless the effect upon the moduli is marked. Fig. 3 shows Young's modulus plotted against density and the shear and bulk moduli show a similar variation: a substantial increase is obtained in all cases.

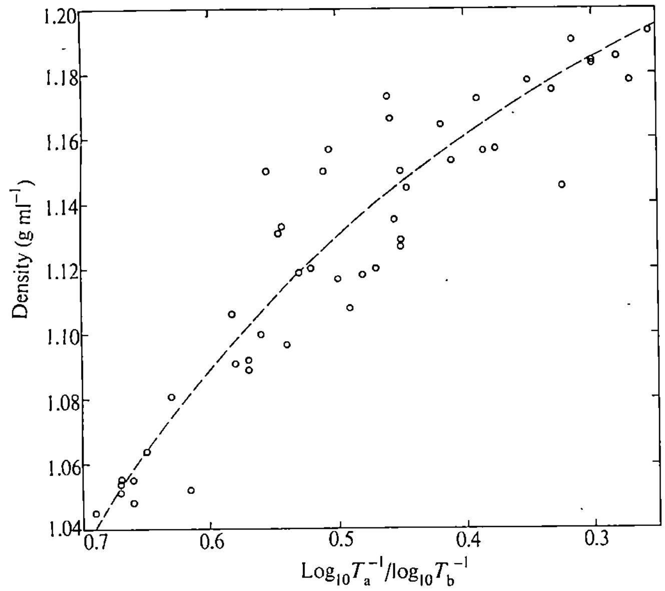

Fig. 2 Plot of density of poly(*p*-divinylbenzene) against $\log_{10}T^{-1}_{901\ \text{cm}^{-1}}/\log_{10}T^{-1}_{837\ \text{cm}^{-1}}$ ($\propto$[residual vinyl group]).

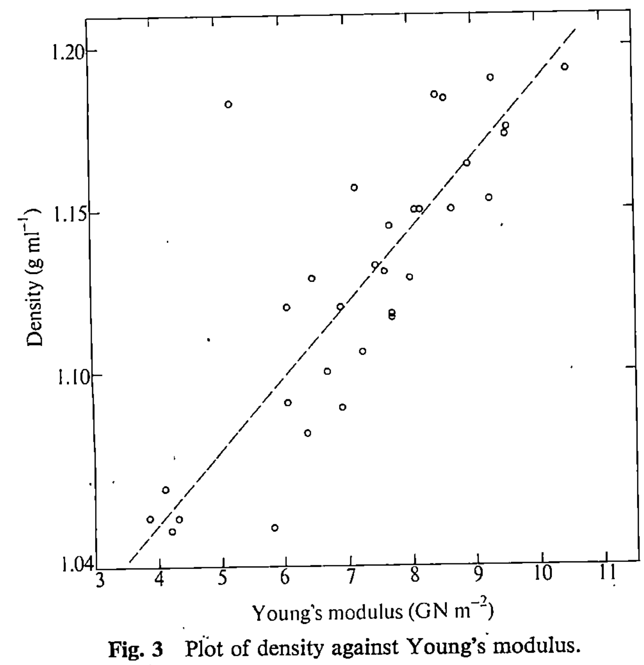

Fig. 3 Plot of density against Young's modulus.

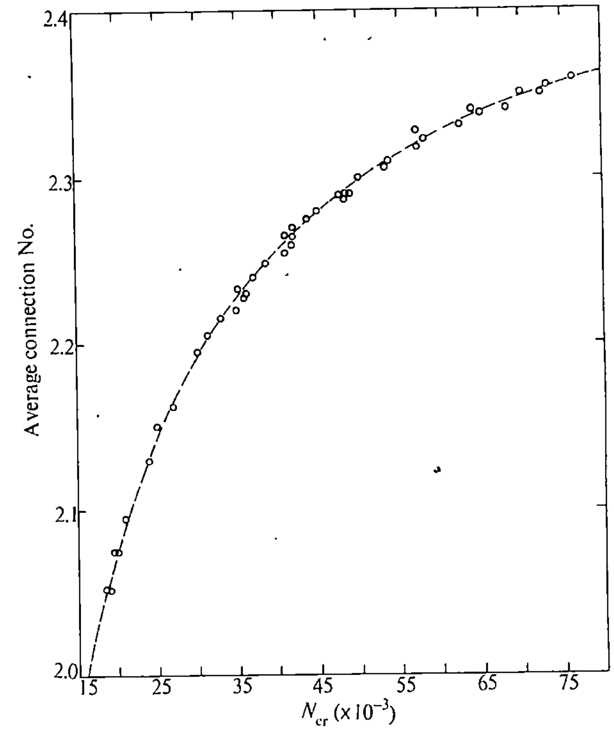

Fig. 4 Plot of average connexion number of *p*-divinylbenzene polymers against N_{cr}.

The concept of connexion number[6], which provides a means of describing regular covalent networks, has been adapted to random polymer networks[2]. The maximum average connexion number of poly(*p*-divinylbenzene) is 2.4 while that of the densest of our products is about 2.36. More recently a new parameter N_{cr} has been introduced[7]; it is the relative number of covalent network bonds per unit volume in a polymer. Fig. 4 shows a plot of connexion number against N_{cr} for all polymerizations.

The *p*-divinylbenzene system, though a convenient model, is unsuitable for the preparation of practically useful materials. It is unlikely for steric reasons that any appreciable further increase in average connexion number could be achieved even at much greater pressures and, in addition, the products are extremely brittle. However, a few experiments with mixtures of *p*-divinylbenzene and *p,p'*-divinyldiphenyl ether have shown the same trend with the production of less brittle materials and it seems likely that with careful choice of polyfunctional monomer the theoretically possible average connexion number might be more closely approached and that practically useful materials might be obtained.

We thank Professor R. N. Haward for discussions.

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Icelandic Geothermal Activity and the Mercury of the Greenland Icecap

A RECENT controversy over mercury found in Greenland ice cores[1-3] has served to underscore the need for more information about natural sources and modes of dissemination of the element.

Following the demonstration of high levels of atmospheric mercury in Hawaiian thermal areas[4], similar aerometric studies were conducted at a number of sites in Iceland during June and July 1972. Field air sampling procedures and analyses by flameless atomic absorption were carried out as described in the Hawaiian study.

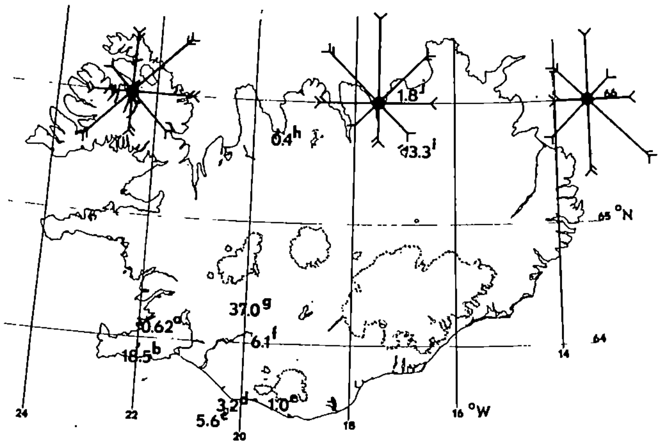

Fig. 1 Aerometry of mercury in Iceland. Located on the outline map are the atmospheric mercury levels (in $\mu g\ m^{-3}$) in June and July 1972, and representative wind vector ("windrose") patterns for June 1972. Mercury sampling sites were: a, Reykjavík; b, Krýsuvik; c, Surtsey; d, Heimaey; e, Solheimajökull; f, Hekla; g, Geysir; h, Varmahlid; i, Myvatn; j, Húsavík.

Although atmospheric mercury levels vary greatly according to site, samples from several widely separated locations (Fig. 1) yielded Hg concentrations well above the range commonly cited for unpolluted air[5], 0.001–0.010 $\mu g\ m^{-3}$. The general reliability of field measurements is indicated by samples taken at the Krýsuvik thermal area where duplicate analyses on each of four separate sample traps yielded a mean value of 11.3 $\mu g\ m^{-3}$ and a standard error of only $\pm 1.8\ \mu g\ m^{-3}$. In the Westmann Islands (including Surtsey), five sites yielded a mean Hg level of $2.4 \pm 0.8\ \mu g\ m^{-3}$.

Atmospheric mercury may be introduced in part by degassing of fluid magmas, but release from fine ash could also serve as a vehicle. Thus, an acid condensate from Surtsey yielded on analysis 350 p.p.b. Hg and tephrafines collected in the first two hours of the 1970 Hekla eruption contained 375 p.p.b. of readily water-soluble Hg.

Long range transport of volcanic ejecta eastward from Iceland is well established. Thorarinsson[6,7] notes that in 1947, tephra was deposited in Finland, some 3,000 km distant, two days after Hekla began its great eruption; and that the vast gas emission accompanying the Lakagigar eruption of June 1783 caused a blue haze which spread for months over all of Iceland, most of Europe and proximal parts of Africa and Asia. Although these episodes show the feasibility of atmospheric transport, advection from Greenland to Iceland would be favoured by prevailing westerly winds. Examination of North Atlantic wind vector patterns[8] (Fig. 1) show that the winds (in June, for example) may blow as much as 30–50% of the time from east to west across Iceland toward Greenland. Furthermore, North Atlantic gales, which are commonly associated with eastward moving cyclones, sustain a westward circulation in their northern sectors, and provide additional means for conveying effluents from Iceland to Greenland[9].

The presence of substantial Hg levels in deep North Atlantic sediments located S, SW, and W of Iceland[10] may also reflect long term transport and fallout of Icelandic mercury in nearby waters[9].

Whatever may be the significance of time-variable mercury levels, they cannot be viewed as evidence for human input when it is recalled that from the mid-17th century to the present, Iceland has recorded nearly 50 volcanic eruptions including some of the greatest in the post-glacial history of the Earth.

We thank Dr Gudmundur E. Sigvaldason and the Division of Geosciences at the University of Iceland for generous laboratory facilities and cooperation in field collection and sampling. This work was supported in part by the National Aeronautics and Space Administration, the Cottrell Foundation of the Research Corporation, the University of Hawaii Foundation, and the University of Hawaii Environmental Center.

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Distribution of Dissolved Mercury in the Irish Sea

PRESTON *et al.*[1] have recently examined the distribution of a number of heavy metals in British coastal waters. They have found that the average concentrations of these elements in waters and marine organisms were significantly higher in samples from the eastern Irish Sea than in those from other areas. Fish and shellfish from this region (particularly the Mersey Estuary and Lune Deep) have been observed to have the highest average contents of mercury of any from around the British Isles[2]. No data are available for the concentration of the element in the seawater of the Irish Sea, nor is anything known about whether significant mercury pollution arises from liquid wastes discharged into the sea from the populous, highly industrialized areas of Lancashire. Trade effluents from the many chemical and industrial plants (including three chlorine–alkali works) would probably be the principal sources of mercury, but the input from sewage, which may contain a significant concentration of mercury (2–150 p.p.m. on the dry weight)[3,4], would also be important, as the total daily discharge of (mainly untreated) sewage to the area amounts to about 0.7×10^6 m^3 (ref. 3). We describe here the distribution pattern of dissolved mercury in the Irish Sea, and have demonstrated that significant pollution occurs in the eastern coastal strip.

Six cruises were made between July 1971 and September 1972 to collect surface waters in an area east of a line between St. Bees Head and Anglesey. In addition, a surface water sampling programme was carried out in September and October 1972 covering the remainder of the Irish Sea. Immediately after collection, the sample (2.5 l.) was filtered through a treated membrane filter (pore size 0.45 μm) and the first 500 ml. of filtrate was rejected. The remainder of the filtrate was acidified to 0.2 M with sulphuric acid and transferred to silicone-coated glass bottles for transport to the laboratory. Tests showed that <20% of the dissolved mercury was lost during the filtration, and that the acidified samples could be stored safely for several weeks. A combination of dithizone extraction and cold vapour atomic absorption spectrophotometry[5] was used for the analysis of the samples. Organic forms of mercury such as methyl mercury as well as inorganic mercury are determined by this technique[6].

The survey carried out in September–October 1972, showed (Fig. 1) that excluding the coastal strip about 40 km wide extending northwards from Anglesey, the dissolved mercury content of the Irish Sea lay almost entirely in the range 25–50 (average 32) ng l.$^{-1}$ except for the central area in which it ranged from 10–24 (average 18) ng l.$^{-1}$. The overall range of values is similar to that found for the English Channel[7], the northern North Sea[8], and the NE Atlantic[9].

The six surveys of the eastern coastal strip showed a consistent picture (Fig. 2). The general levels of dissolved mercury in the inshore waters are similar to those found in the westerly regions examined in the cruise in September–October. These concentrations probably represent the equilibrium values for the distribution of mercury between water and suspended matter. Offshore, there are two areas in which the dissolved mercury concentration exceeds 200 ng l.$^{-1}$. One of these is in the vicinity of the North West Light, an area which is used for the dumping of sewage sludge from the Manchester conurbation[10].

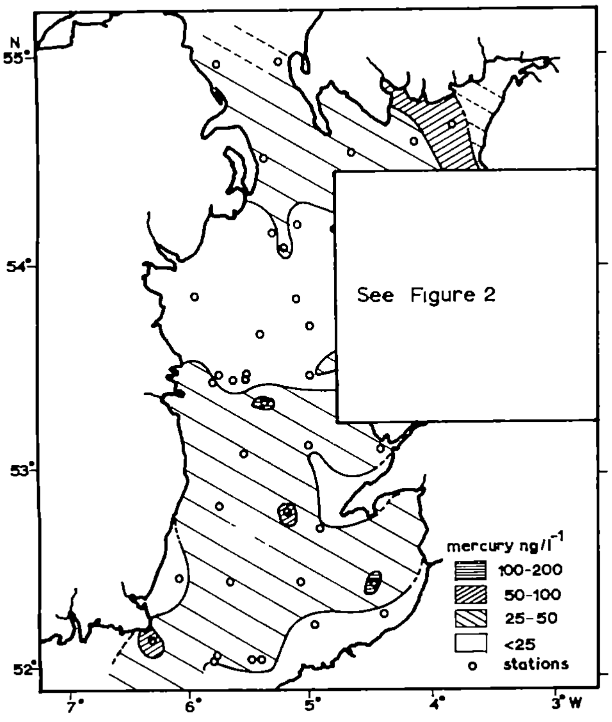

Fig. 1 Distribution of dissolved mercury in the Irish Sea in September–October 1972 (as ng l.$^{-1}$).

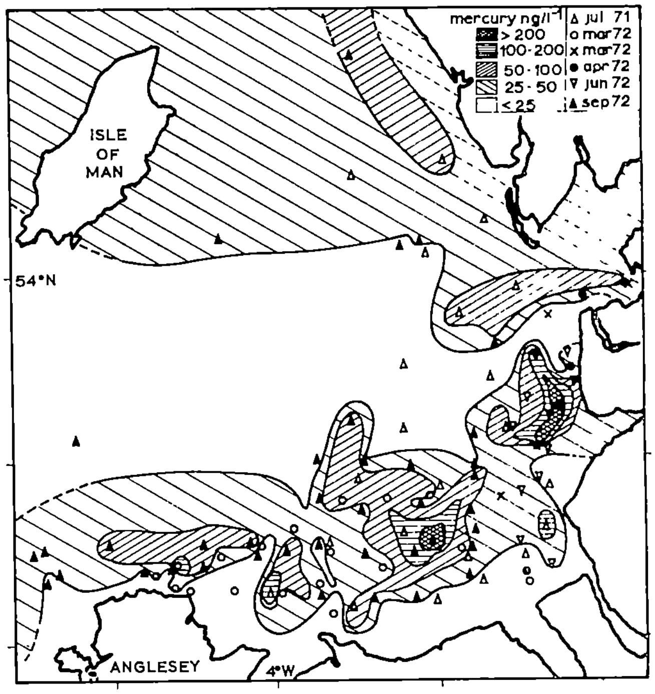

Fig. 2 Distribution of dissolved mercury in the eastern coastal area of the Irish Sea (as ng l.$^{-1}$).

Dried sludges are known to contain up to 150 p.p.m. of mercury and, in fact, concentrations of particulate mercury of up to ~900 ng l.$^{-1}$ were observed in the area. We tentatively suggest that the observed high concentrations of dissolved mercury found at this station were liberated during bacterial decomposition of the sludge. The dissolved mercury content is also relatively high in an elongated patch to the west of the Ribble Estuary. The highest concentration observed in this region was 443 ng l.$^{-1}$, but the source of the pollution in this area is uncertain. In view of the very low levels of dissolved mercury to the north, it seems very unlikely that it originates from effluents from the ICI chlorine–alkali plant on the River Wyre. It is probably significant that these two areas lie within that part of the Irish Sea yielding fish which have an average mercury content (0.53 p.p.m. dry weight) more than double those from the rest of this sea (average 0.21 p.p.m.)[2].

We thank Drs T. R. S. Wilson and P. R. Hinchcliffe for their assistance in the sampling programme.

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BIOLOGICAL SCIENCES

Localization of Paternal DNA in Interphase Nuclei of Mouse Eggs during Early Cleavage

TRANSFER of labelled paternal genome has been demonstrated during fertilization in mammals[4,5,14,15]. The ^{14}C adenine used, however, did not permit precise localization of parental material within the nuclei of the dividing egg. These and other observations using tritiated thymidine (^{3}H-TdR)[8] were made on histological sections of eggs, limiting the precision of the localization of the entire paternal DNA complement in egg chromatin. Intense labelling of the germinal cell line in male mice has been described, using ^{3}H-TdR[7,11], and we have combined this by using the air-drying method of Tarkowski[16] (which gives good preparations of complete egg nuclei) to localize the paternal DNA complement.

Male mice (inbred CBA T6/T6 strain) were injected intratesticularly with ^{3}H-TdR[11]. They were mated with females, superovulated with gonadotrophins[6], on the day of peak-production of labelled spermatozoa, as shown by 50% labelled epididymal sperm, or sperm collected by vaginal washings shortly *post-coitum*[13]. This was found to be 32 to 34 day[1,7,9]. The time of mating was calculated from the time of appearance of a vaginal plug. Females were killed from 36 to 60 h post-mating, corresponding to two to eight cells in the cleavage stages of the egg[3], and were given colchicine 1.5 to 2 h before death[16]. Oviducts were dissected and eggs collected with a micropipette under a dissecting microscope by flushing with Hanks medium. After 6–8 min in hypotonic citrate, eggs were fixed with one drop of acetic alcohol (1 : 3), air-dried and treated with a further two drops of fixative at the beginning of spreading[16]. Autoradiographs (ARG) ('Kodak NTB-2' or 'Ilford L-4' dipping emulsion) were exposed for 60 day and stained through the film with 2% toluidine blue.

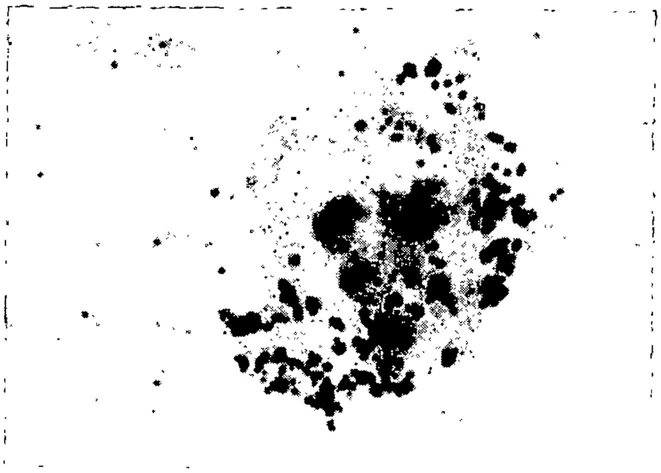

Fig. 1 Patchy and polar localization of ^{3}H-TdR grains in a nucleus from a 4 cells stage egg fertilized with labelled sperm.

When mating occurred at the peak of radioactive sperm production, approximately 30 to 50% of labelled eggs were recovered from a given female. ARG's of eggs fixed at the pronuclei stage revealed labelling of only one pronucleus, usually the larger one. The grains were randomly distributed over the whole nuclear area.

At later stages ARG grains were not randomly distributed and in more than 90% distribution was patchy (Fig. 1). They did not appear to be preferentially localized over any nuclear structure. In almost all labelled nuclei, grains were localized preferentially, the remaining nuclear area being devoid of label. Polar localization of the labelled zone was apparent in 147 out of 368 labelled nuclei, ranging from cleavage stages of two to eight cells. In these nuclei, we evaluated the relative grain proportion of the total nuclear surface. In 30% of nuclei the grains extended over half of the nucleus, in 64% the zone was relatively smaller, and in 6% markedly larger than half the surface. The zone in the remaining two thirds of the labelled nuclei, with no polar localization was more difficult to locate exactly, although label was non-random.

The 220 nuclei were arbitrarily classified in three categories; (*a*) grain distribution in a crescent-like zone at the nuclear periphery (19%); (*b*) a belt-type localization in the central part of the nuclear surface (63%); (*c*) any other type of localization (18%, 1% completely labelled).

We suggest that there is segregation of the chromatin according to parental origin in interphase nuclei of cleaving fertilized eggs. This was particularly apparent in eggs of two to five nuclei, but impossible to assess in later stages because of low intensity of labelling (due to dilution of ^{3}H-TdR) and the small number of eggs.

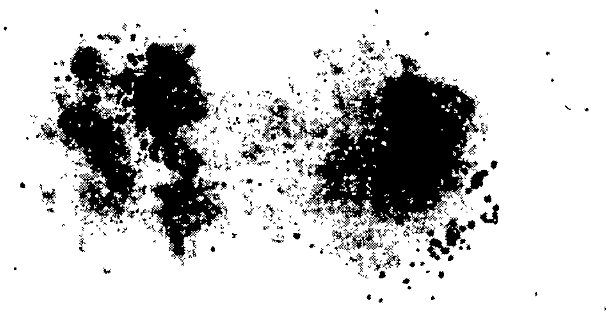

Fig. 2 Two nuclei from a 4 cells stage with different orientation polar localization.

We believe these results are not autoradiographic artefacts because: (1) No localized distribution of grains was seen in controls, namely pronuclei stages or fertilized eggs incubated *in vitro* with ^{3}H-TdR during cleavage[10], (2) orientation of labelled poles was completely different in each nucleus (Fig. 2), eliminating the error of uneven coating with ARG emulsion. We did not analyse the relative position of labelled polar zones of different nuclei in the same egg, however, as phase-contrast microscopy showed distortion of the cellular orientation during fixation.

Radiobiological artefacts cannot be completely eliminated. Lethal mutations were induced by ^{3}H-TdR labelling of sperm[1], related to the degree of labelling. The dominant lethals were only recorded on the thirteenth day of gestation, however, and rates of fertilization and development of the zygote during early stages following *in vitro* fertilization was almost the same for normal and ^{3}H-TdR-labelled sperm[9].

There are two indirect cytological arguments from our work showing there are no major radiobiological lesions of the organization of the egg nuclear chromatin ^{3}H-TdR due to: first, the mean number of ARG grains lying over all nuclei of a given zygote has been determined and compared to the stage of cleavage (from two to six cells). This mean total of 120 grains per egg (range 18 to 411), is not significantly different in any cleavage stage, nor does it diminish with advancing cleavage. We have not been able to analyse the numbers of grains between various nuclei of the same egg with relation to the segregation of labelled material among daughter-cells because of insufficient data. Observed distributions, however, were compatible with an equal segregation of the labelled material, at least during the first division of the zygote. The patterns at later stages can also be explained, considering asynchrony in the divisions of their nuclei; second, in all the 24 labelled metaphases from eggs containing two to seven nuclei, ^{3}H-TdR was localized in a half or less of the chromosome complement. An exact evaluation of the distribution of labelled chromosomes has not been made, but in relative terms, metaphases at the 2 cell-stage tended to approach a Mendelian 1/1 distribution of labelled and unlabelled chromosomes.

We cannot at present make definite conclusion from these data, especially as the degree of labelling of a fertilizing sperm cannot be precisely determined. Some of them were exposed to ^{3}H-TdR only during the late part of the last period of spermatogonial DNA synthesis and although sperm production occurs in waves, a marked mixing in the epididymis is known to occur[12]. The partially-labelled sperms may contribute to the patchy distribution of grains, in their heterochromatic component[2]. Embryologically a topographical separation of paternally-derived nuclear chromatin in early diploid mouse eggs is reasonable. Molecular and genetic implications are that the region of the interface between the two parts leaves ample room for any grouping of allele gene pairs.

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Electron Microscopy of Negatively Stained tRNA

Several techniques have been used to determine the three-dimensional conformation of transfer ribonucleic acid (tRNA), including small angle X-ray scattering[1], electron microscopy[2-5], among other physical[6], chemical and biological methods[7]. Here we report some observations of certain "superstructures" of negatively stained tRNA using electron microscopy.

Transfer RNA samples were from *Escherichia coli* K12 tRNA (General Biochemicals Inc., Ohio) and of yeast phenylalanine tRNA (Boeringer, Manheim, California). The *E. coli* K12 tRNA was specified as having 96% RNA, 2.2% protein, <1% DNA, no RNAase activity, and an absorbancy of 2.0 at 260 mμ in a 0.01% solution. We used the 2% aqueous ammonium molybdate (Fisher Scientific Company, maximum impurities 0.015%) adjusted to *p*H 7.4 or 8.3 with 10 M ammonium hydroxide as a negative stain. Support films of 'Formvar' were thinly coated with carbon in an 'Edwards E12E' vacuum evaporator, and mounted on copper grids. In these experiments 2 mg of tRNA were dissolved in 1 ml. of negative stain and sprayed onto the support film with a glass atomizer to give droplets 5–10 μm in diameter. Some preparations were sonicated for 1 h in a 'Ladd Ultrasonicator' before spraying. All preparations were observed in a 'Philips EM300' electron microscope operated at 80 kV. Photographs were taken on 'Ilford EM5' plates and developed in 'Ilford 1D2'.

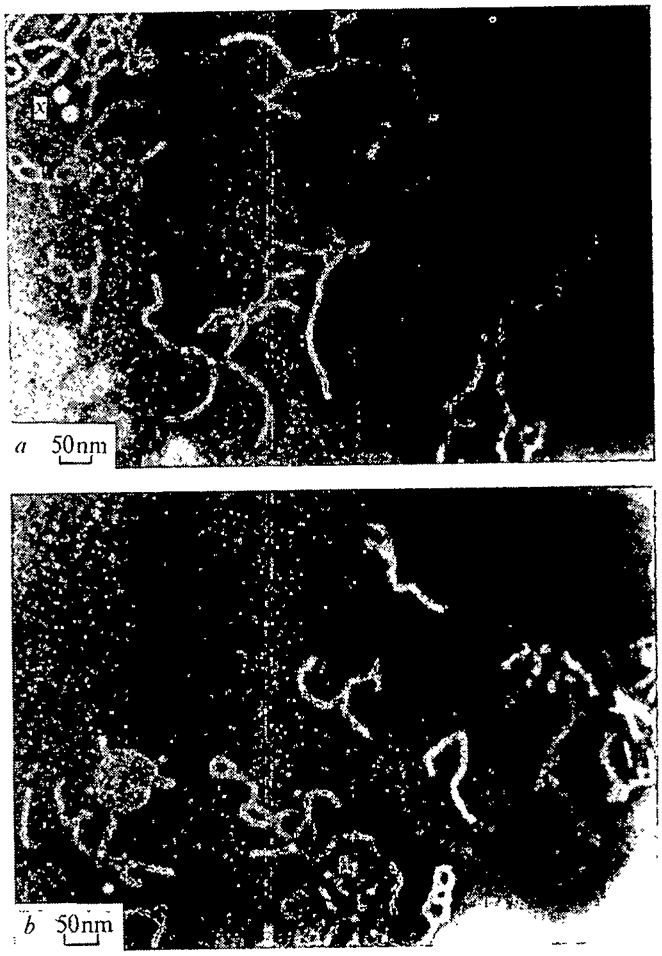

Fig. 1 *a*, tRNA negatively stained with 2% ammonium molybdate at *p*H 7.4, showing long branching "worm-like" structures 2 to 13 nm thick with two solid circular areas (*x*). *b*, As *a*, with *p*H 8.3. The thickness of the structures is more variable and one extensive sheet is seen.

In unsonicated preparations of *E. coli* tRNA at both *p*Hs, long "worm-like" structures up to 0.5 μm in length were seen abundantly in most droplets of negative stain. These structures were not seen in any droplets of negative stain alone, in negatively stained yeast phenylalanine tRNA, or in sonicated preparations of negative stained *E. coli* tRNA; or were they found in *E. coli* tRNA samples which had been incubated in ribonuclease (5 × cryst., bovine pancreas, A grade, Calbiochem) for 48 h at 37° C before negative staining.

At *p*H 7.4 (Fig. 1*a*) these structures were seen to be of quite constant thickness (12 to 13 nm) They were usually curved, with a minimum inner radius of curvature of 4 nm and branched frequently; always into two, and usually symmetrically at 120°. Often these branches formed closed loops. Occasionally solid circular areas about 25 nm in diameter were seen whose density resembled areas where two of the "worm-like" structures overlapped.

At *p*H 8.3 (Fig. 1*b*) these structures demonstrated some striking differences. They were more varied in thickness, occasionally spreading out into sheet-like areas of varied diameter, and closed loops were more frequent. All of these structures, as well as the thinner areas of negative stain, showed a mottled density pattern which was different from the 1.0–1.5 nm granularity of both the carbon-'Formvar' support film and the negative stain without tRNA.

The presence of these structures in these preparations indicates extensive aggregation of tRNA molecules in a specific manner. This aggregation could involve differences in the primary structure of the tRNA molecules, as the structures did not occur when only one species (phenylalanine tRNA) was present. The forces holding the aggregates together are not strong, because sonication disrupted the structures. To form chains or sheets of molecules, more than one site of interaction must exist on each molecule.

The two sites of chemical bonds in the cloverleaf model[8] of the tRNA molecule which would satisfy these criteria are: *a*, hydrogen bonding between looped regions of adjacent molecules as demonstrated by Eisinger[9]; *b*, base pairing between 3′ and 5′ ends of partially separated stems of adjacent molecules, as suggested by Fröholm and Olsen[2–4]. It is likely that both of these types of interaction exist, as well as some interaction with the negative stain itself.

The worm-like structures are unlikely to be cylinders or rods, as their edges appear too sharp, but they could be flat sheets or flattened cylinders. In this case the molecules are arranged about the surface of the structures as this would allow formation of extensive sheets at the higher *p*H used here[2,3]. If, however, the structures are rods or cylinders, the molecules can be arranged along the axis of the rod. Dimers of tRNA have been described with a length of 10.9 nm[5], which is in agreement with the observed 12–13 nm thickness of our preparations. The dimers could be in a rosette arrangement along the rod axis.

The mottle fine structure of these rods or sheets, as well as of the thinner areas of negative stain, is a ring of 3–4 nm, but no definite arrangement of these could be determined. We are now studying this fine structure in greater detail.

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Preliminary X-ray Analysis of the Crystalline Complex between Poypeptide Chain Elongation Factor, Tu, and GDP

DURING protein synthesis in bacteria, aminoacyl tRNA is transported to the ribosome complexed with a protein elongation factor Tu (EF-TU) and GTP[1–3]. In the ribosome the aminoacyl tRNA is positioned onto its appropriate codon, GTP is hydrolysed, and EF-Tu is released as a stable complex with GDP. The EF-Tu·GDP complex is then reconverted to EF-Tu·GTP by means of another soluble protein, EF-Ts. Transfer factors analogous to EF-Tu but with different physical properties have also been isolated from eucaryotic systems. The EF-Tu·GDP complex has been purified to homogeneity from *Escherichia coli*[4,5]. The protein factor has a molecular weight around 40,000 and is composed of a single polypeptide chain. It forms a stable 1 : 1 complex with GDP which has a dissociation constant of 3×10^{-9} M[4]. In the purification of EF-Tu from *E. coli*, needle shaped microcrystals have been reported[4,5] on addition of ammonium sulphate; these crystals were too small for X-ray diffraction analysis, however. Here we report the preparation of large crystals of an EF-Tu·GDP complex and describe their preliminary analysis by X-ray diffraction.

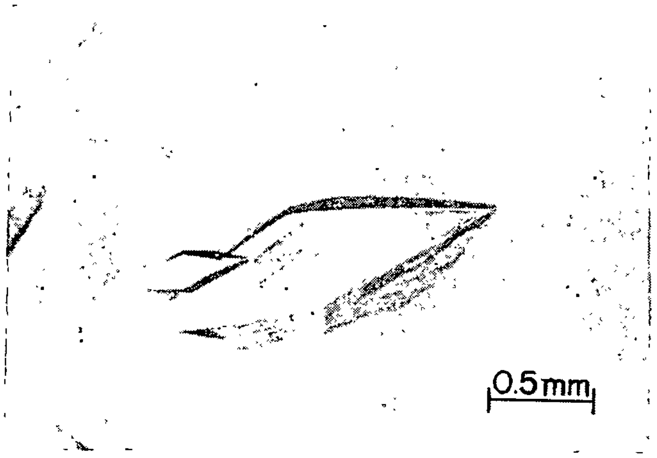

Fig. 1 Microphotograph of crystals of Tu·GDP complex. Crystals are found with both smooth and irregular faces.

We have prepared purified EF-Tu·GDP by methods described previously[4]. Larger crystals were obtained by using a method of vapour phase equilibration similar to that used for tRNA crystals[6]. A solution was prepared containing 14 mg ml.$^{-1}$ EF-Tu·GDP, 10 mM Tris·SO_4 (*p*H 8.0), 0.5 mM dithiothreitol, 0.5 mM $MgSO_4$, 1 mM $MgCl_2$, 0.05 mM EDTA and 0.01 mM excess GDP. 40 µl. aliquots of this solution were put into the depressions of a 'Pyrex' spot plate which was then placed on a platform in a plastic box. A reservoir of 25 ml. of 2% isopropanol was placed into the bottom of the plastic box which was then sealed and stored at 4° C. Crystals began to appear after approximately one month. This was associated with a vapour phase equilibration of the isopropanol as well as some evaporation of the crystallizing solution. Crystals have also been obtained with up to 10 mM $MgCl_2$ or with a reservoir containing 2-methyl-2,4-pentanediol rather than isopropanol. These crystals appear with either the morphology shown in Fig. 1 or as tetragonal bipyramids.

The crystals were mounted in thin-walled glass capillaries together with a droplet of mother liquor for X-ray diffraction analysis. Twelve degree precession photographs with a crystal to film distance of 100 mm were taken for approximately 48 h

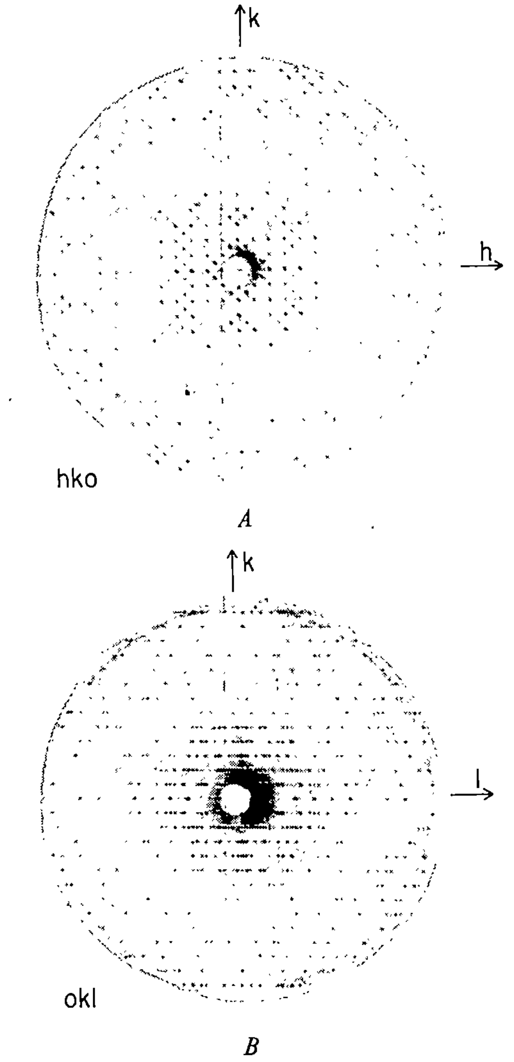

Fig. 2 Precession photographs of Tu·GDP crystals. The precession angle was 12° and the exposure near 50 h. The *hk*0 (*A*) and 0*kl* (*B*) projections are shown. The *pseudo* fourfold axis is perpendicular to the *hk*0 projection.

at 8° C using Cu$K\alpha$ radiation from an 'Elliot' rotating anode source.

Two projections are shown in Fig. 2. The cell is c-centred, orthorhombic, and has dimensions $a=98.2$ Å, $b=100.1$ Å, $c=160.6$ Å. The space group is $C222_1$. There is a full representation of diffraction intensity out to at least 2.8 Å, making them quite suitable for detailed X-ray analysis. The crystals are stable in the X-ray beam for around one week.

The high *pseudo*symmetry is readily apparent from inspection of the *hk*0 and 0*kl* projections (Fig. 2). Examining the 001 axis, only every fourth reflexion appears, implying the presence of a fourfold screw axis. In the limit of resolution of these photographs there is no sign of a reflexion other than $l=4n$ appearing. However, the *hk*0 projection does not have true fourfold symmetry. The *pseudo*symmetry corresponds to the tetragonal space group of $P4_12_12$ with cell dimensions $a=b=70.2$ Å, $c=160.6$ Å, $\gamma=91°\ 12'$ and a volume of one half that of the true orthohombic unit cell. The density of the crystal measured in a density gradient is 1.20 g ml.$^{-1}$. Assuming that EF-Tu·GDP has the partial specific volume of 0.74 g ml.$^{-1}$, which is an average value for most proteins, and the density of the mother liquor to be 1.02 g cm^{-3}, the protein occupies 55% of the unit cell volume. There are two molecules per asymmetric unit and these molecules are related by a *pseudo* fourfold screw axis along the *c* axis.

The protein, EF-Tu, is of interest because it is capable of interacting with guanosine nucleotides, all aminoacyl tRNA's with the exception of met-tRNA$_{F}$, and with EF-Ts as well as some portion of the ribosome-mRNA complex. Structural studies of these complexes by X-ray diffraction may reveal details of the protein-nucleotide interactions and may also illuminate the currently unknown mode of action of the protein. We are trying to obtain suitable isomorphous derivatives of these crystals, and crystals of this protein complexed to aminoacyl-tRNA.

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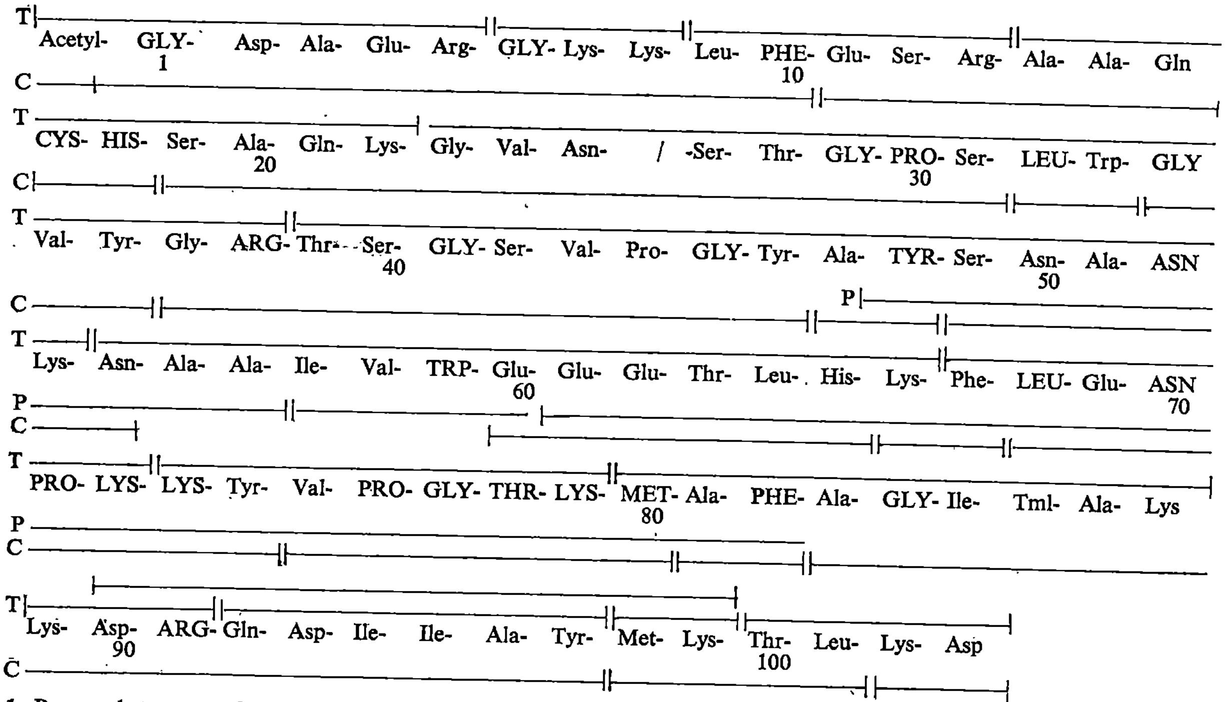
The Amino-acid Sequence of Cytochrome c from *Euglena gracilis*

THE large number of mitochondrial cytochrome c sequences known and the elucidation of the tertiary structure of the horse heart protein by Dickerson's group[1] provide a good opportunity for studying the evolution of a molecule and for correlating structure with function. Dickerson has shown that relating sequence data to the tertiary structure can generate hypotheses about functional regions that are evolutionarily conserved. There is no general agreement, however, as to whether the differences in sequence from different species are adaptive or neutral and this is an aspect of the current selectionist versus neutralist argument[2].

A few protozoan cytochromes c have been purified[3-7]. From an evolutionary point of view, sequences of proteins from these organisms may be interesting, as they are considered the most ancient eukaryotic group and their proteins may provide homology links with prokaryotes. Such links could suggest a history for the organelle in which the protein is found. (The interpretation of this kind of evidence may not be simple: cytochrome c, for example, is found in the mitochondrion but in present-day eukaryotes is thought to be coded for in the nuclear genome[8].) The phylogenetic origin of the Protozoa may be complex, with the possibility of algal derivation along different lines of descent at different times in the evolutionary past.

The sequence of cytochrome c (C557) from the flagellate, *Crithidia oncopelti*, has been reported[9] and I present here the proposed sequence of cytochrome c (C558) from the photosynthetic flagellate, *Euglena gracilis* (Fig. 1). The protein was purified and apoprotein was prepared in the same way as cytochrome C557. Enzymic digestion was performed on

1–1.5 µmol quantities of apoprotein and peptides were separated using conventional techniques[10]. The dansyl-Edman procedure[11] was used to identify all the residues except the tryptophans and the N-terminal region. Spectrophotometric examination[12] indicated two tryptophan residues per mol and there were two Ehrlich-positive tryptic peptides (Gly_{23}-Arg_{38} and Asn_{54}-Lys_{66}). The tryptophan residues were positioned on the evidence of sub-digests of these two peptides and carboxypeptidase A experiments.


T
Acetyl- GLY- Asp- Ala- Glu- Arg- GLY- Lys- Lys- Leu- PHE- Glu- Ser- Arg- Ala- Ala- Gln
1
10
C
T
CYS- HIS- Ser- Ala- Gln- Lys- Gly- Val- Asn- / -Ser- Thr- GLY- PRO- Ser- LEU- Trp- GLY
20
30
C
T
Val- Tyr- Gly- ARG- Thr- -Ser- GLY- Ser- Val- Pro- GLY- Tyr- Ala- TYR- Ser- Asn- Ala- ASN
40
50
C
P
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Lys- Asn- Ala- Ala- Ile- Val- TRP- Glu- Glu- Glu- Thr- Leu- His- Lys- Phe- LEU- Glu- ASN
60
70
P
C
T
PRO- LYS- LYS- Tyr- Val- PRO- GLY- THR- LYS- MET- Ala- PHE- Ala- GLY- Ile- Tml- Ala- Lys
80
P
C
T
Lys- Asp- ARG- Gln- Asp- Ile- Ile- Ala- Tyr- Met- Lys- Thr- Leu- Lys- Asp
90
100
C

Fig. 1 Proposed structure of cytochrome c from *Euglena gracilis*. Peptides from tryptic (T) and chymotryptic (C) digests are shown. Invariant sites are in capital letters. Tml=Trimethyllysine. /=deletion. Some peptic peptides (P) are included.

The peptide (Gly_{23}-Arg_{38}) did not always give clean results during Edman degradation, due perhaps to acidolysis in the Ser-Thr-Gly sequence. Because of the deletion and the tryptophan in this peptide several independent proofs of its sequence were obtained. The blocked N-terminal peptide was partially hydrolysed in acid and the products were separated and identified. The acetyl group was confirmed after hydrazinolysis as dansyl-acetyl-hydrazine[13].

Some regions of single residue overlap between tryptic and chymotryptic peptides were confirmed by digestion of the protein with pepsin. The relevant peptides are included in Fig. 1 and are assigned on the basis of amino-acid composition, N-terminal and C-terminal studies only. Amides were located by examining the mobilities of parent peptides, of sub-digest peptides or of remainder peptides during Edman degradation. The amino-acid composition of the protein is in good agreement with the sequence (Table 1).

The mid-point potentials of cytochrome C557 and C558 were measured by the method of Davenport and Hill[14] with ferro-ferricyanide buffers in an anaerobic cuvette. *Pseudomonas* c_{551} and horse heart cytochrome c gave values in fair agreement with literature results (284 mV compared to 282 mV found by Horio[15] for c_{551} and 267 mV compared to 261 mV found by Schejter[16] for the horse heart protein). Cytochrome C557 was determined as 264 mV and C558 as 244 mV.

Like cytochrome C557, the *Euglena* protein has distinctive spectral properties[6,7]. Meyer has already suggested an atypical haem binding on the basis of the pyridine ferro-haemochrome which has an absorption maximum at 553 nm. This is intermediate between the 550 nm of all other c-type cytochromes and the 556–558 nm of proteins containing protohaem IX.

Residue 14 in cytochrome C558 is alanine in place of cysteine. The haem appears to be bound through only one covalent link leaving one vinyl group unsaturated. Cytochromes C557 and C558 are, at present, unique amongst haemoproteins in having this prosthetic structure.

Cytochromes C557 and C558 are not closely related. Out of 103 positions compared, 48 are different. Nor is cytochrome C558 close to wheat cytochrome c; they have 52 differences. Table 2 suggests that a saturation effect occurs at large evolutionary distances and that the cytochrome c molecule becomes unreliable in defining times of divergence. The structural constraints imposed by functional requirements apparently make this saturation level about half the total number of residues.

The N-terminal sequences and the pattern of methylation of

Table 1 Amino-acid Composition of *Euglena gracilis* Cytochrome c

	Composition	Sequence
Aspartic acid	9.2	9
Threonine	4.85	5
Serine	6.85	7
Glutamic acid	9.0	9
Proline	4.25	4
Glycine	9.65	10
Alanine	11.8	12
Valine	5.0	5
Methionine	1.95	2
Isoleucine	3.95	4
Leucine	4.95	5
Tyrosine	4.8	5
Phenylalanine	3.0	3
Histidine	1.95	2
Lysine	11.9	12
Trimethyllysine	1.0	1
Arginine	4.1	4
Cysteic acid	0.9	1
Tryptophan	1.9	2

Composition based on residues/iron atom and compared with total residues in the proposed sequence.

Aliquots of the same solution were used for 20 and 90 h hydrolyses and for iron determination[21]. Cysteic acid was estimated separately after removal of the haem and performic acid oxidation. Tryptophan was estimated by the Goodwin and Morton method[12].

cytochrome c roughly fit phylogenetic categories. The cytochromes c of vertebrates are acetylated at Gly$_1$: those of invertebrates and ascomycetes have free and slightly extended N-termini; and those of plants are acetylated at Ala$_{-8}$. Trimethyllysine was found at residues 72 and 86 in plant cytochromes c, 72 in ascomycete cytochromes c and not at all in others[17].

Table 2 Amino-acid Differences

	Horse	Wheat	*Neurospora*	Yeast	*Euglena*	*Crithidia*
Horse	0	46	46	46	45	46
Wheat	46	0	54	47	52	48
Neurospora	46	54	0	41	48	58
Yeast	46	47	41	0	56	51
Euglena	45	52	48	56	0	48
Crithidia	46	48	58	51	48	0

Only those positions common to all were compared.

Neither cytochrome C557 nor C558 fits into these categories. The former has a nine residue extension which is blocked at the amino terminus and residues–8 and 72 are methylated. The latter is acetylated at Gly$_1$ like the vertebrate cytochromes and Lys$_{86}$ is methylated.

The deletion at residue 25 in cytochrome C558 is the first example of an internal deletion in a cytochrome c and nearby Lys$_{27}$ is replaced by a serine. The X-ray structure shows this region as a hairpin loop[1] and perhaps the folding of this loop in cytochrome C558 is different from that of horse heart.

The elucidation of the sequence of cytochrome C557 reduced the number of common residues in the cytochrome c family from 33 to 29. Cytochrome C558 has a novel variation at residue 67 where a phenylalanine replaces a tyrosine. This is the tyrosine that is preferentially nitrated in horse heart cytochrome[18]. Three changes which were new variations in cytochrome C557 also appear in C558. Lys$_{27}$ is replaced by Ser, Ile$_{75}$ by Val, and Cys$_{14}$ by Ala.

There are now 28 common sites, four below the minimum proposed by a number of people on statistical grounds or guesswork. Dayhoff[19] predicted 14 which could prove to be a more realistic estimate.

Cytochromes c are claimed to be functionally equivalent on three grounds; their ability to restore respiration in mitochondria depleted of their own cytochrome c[20], their reactivity with cytochrome oxidase[20], and the thermodynamic parameters of oxidation and reduction[16]. This evidence has been used to support an interpretation of cytochrome c evolution by neutral mutations. However, Hill *et al.*[3] have shown that *Crithidia fasciculata* cytochrome c reacts more slowly than other eukaryotic cytochromes c with mammalian cytochrome oxidase.

The redox potential of 244 mV for cytochrome C558 determined in this work differs greatly from the 307 mV reported by Perini *et al.*[6]. There is no obvious explanation for this discrepancy. It does appear, however, that cytochrome C558 has a substantially different redox potential from the other mitochondrial cytochromes c studied. Cytochrome C558 thus may not be a member of the functionally equivalent group proposed by Margoliash *et al.* Such an assumption of equivalence may not be justified in any case since too little is known of the detailed role of cytochrome c. The protein cannot be tested thoroughly enough *in vitro* to be confident that changes in its structure are selectively neutral.

These results suggest that cytochromes c may not be so invariant in structure as was anticipated. One of the residues which bind the haem group may change and three positions in the long conserved region preceding Met 80, the sixth haem ligand, are also variable. *Euglena gracilis* cytochrome c may also have slightly different enzymic properties.

One of the possibilities mentioned in the introduction, a homology link with prokaryotes, was not realized. Work is proceeding in this laboratory on cytochrome *f* from *Euglena* and from *Porphyra tenera* and preliminary results suggest that this protein may provide such a link (R. P. Ambler and G. Pettigrew, unpublished observations).

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The Properties and Amino-acid Sequence of Cytochrome c from *Euglena gracilis*

CYTOCHROME c, by virtue of its relatively slow evolution and the large number of sequences already determined, is particularly well suited for investigating the phylogenetic relationships among major taxonomic groups, including the relationship of the protozoans to the metazoans. Among the metazoans, more than fifty cytochromes c have been sequenced from fungi, plants, insects and vertebrates. Already one protozoan sequence has been determined, that of *Crithidia oncopelti*[1], and here we describe a second, from the protozoan, *Euglena gracilis*.

A strain of *Euglena gracilis* was grown in the dark at 25° C with rotary shaking in 6 l. Erlenmeyer flasks containing 2 l. of Difco *Euglena* broth supplemented with 1% (w/v) glucose. The cells freed from chloroplasts were harvested at end of log phase growth by centrifugation for 5 min at 1,000g. Generation time was about 9 h. Recoveries were from 30–50 g wet weight l.$^{-1}$

of medium. Cells were also grown at 30° C in 150 l. batches on a medium containing 1.5% (w/v) glucose, 0.8% (w/v) soy peptone (any peptone seems to work) and salts as defined by Greenblatt and Schiff[2] (G. E. Tarr, personal communication). The *p*H was adjusted to 3.8 with concentrated HCl and aeration and mixing accomplished by sparging with air. Yield was 25 g (wet weight) l.$^{-1}$. Cells were frozen immediately after collection.

Table 1 Composition of *Euglena gracilis* Cytochrome c 558

Amino-acid	Composition by 20 h hydrolysis	Sequence
Alanine	11.4	12
Arginine	3.5	4
Aspartate	9.9	4
Asparagine		5
Cysteine	—	1
Glutamate	9.4	6
Glutamine		3
Glycine	11.6	10
Histidine	1.9	2
Isoleucine	2.9	4
Leucine	5.4	5
Lysine	12.6	13
Methionine	1.6	2
Phenylalanine	3.6	3
Proline	4.2	4
Serine	7.2	7
Threonine	5.1	5
Tryptophan	—	2
Tyrosine	3.3	5
Valine	5.5	5
Total	99.1	102

The 20 h hydrolysis set arbitrarily to total 99 residues. Isoleucine is low because of the resistance if Ile-Ile bond between residues 94 and 95.

15 kg of cells was thawed and suspended in 3 volumes of 8 mM, *p*H 7, NaPO$_4$ buffer containing 0.2 M NaCl. Cells were disrupted by sonication of 800 ml. aliquots in the presence of 5 μm glass beads. Breakage was > 80% within 15 min. The sonicated suspension was brought to *p*H 4.2 with glacial acetic acid, let stand for 30 min and centrifuged The supernatant was adjusted to *p*H 7 with concentrated ammonium hydroxide, ammonium sulphate added to 55% saturation, let stand for 1 h, centrifuged and the supernatant dialysed and recentrifuged. The cytochrome c of the dialysed supernatant was batch-absorbed on 'Amberlite CG-50', washed with *p*H 7, 0.02 M NaPO$_4$ buffer, then eluted with the same buffer but containing 0.5 M NaCl and the volume reduced by pressure dialysis. The procedure beginning with ammonium sulphate was repeated except that it was brought to 60% saturation, the cytochrome oxidized with a few grains of $K_3Fe(CN)_6$ before applying to the 'Amberlite', and a linear ionic gradient used for elution. The cytochrome appeared at a salt concentration of 0.28 M although this will vary, not only as a function of the *p*H, but also as a function of the ratio of column volume to buffer volume in the mixing chambers. Gel filtration on 'Sephadex G-75' gave minimal improvement. The cytochrome, in 5 mM Tris-HCl buffer *p*H 8.37, was applied to a DEAE-cellulose column and eluted with the same buffer. The peak fraction had an OD$_{558}$/OD$_{280}$ of 0.85 and had properties similar to the preparation of Perini *et al.*[3]. Isoelectric focusing was performed with a *p*H 8–10 ampholyte at a final concentration of 0.5% (w/v) plus arginine at 0.1% (w/v) using three different sucrose gradients with a 40% range. The cathode was placed on the bottom with 1% (v/v) monoethanolamine, 1% (w/v) Tris and 1% (w/v) N-ethylmorpholine in 75% (w/v) sucrose while the anode was in phosphoric acid (1/100 v/v) 1 in 100. Cytochrome c was applied in the reduced (by dithionite) form. The column was equilibrated 48 h at a maximum of 1,500 V. Only one band of cytochrome c was obtained and it represented no improvement in purification over the DEAE-cellulose treated product. The isoelectric point was determined by linear extrapolations to zero sucrose concentration. All of the above procedures were carried out at 4° C except the iso-electric focusing which was at 0° C.

A summary of the amino-acid composition and physical-chemical characteristics of cytochrome c is shown in Tables 1 and 2. Ultracentrifugation was performed at 2 concentrations differing by a factor of 10. We have recently also purified *Euglena* cytochrome c by the method of Margoliash and Walasek[4].

The derived amino-acid sequence is shown in Fig. 1. The number of residues that are absolutely necessary for cytochrome c function is of interest. An attempt to estimate this number, using the distribution of substitutions in codons required in their descent to account for known present day sequences, was presented by Fitch and Margoliash[9]. Their results suggested that about 30 of the 35 unvaried positions were invariable. Fitch and Markowitz[10] showed, however, that the number of invariable positions depended on the range of species examined. Within that range, further sequences have since revealed only two additional residues to have had substitutions that survived the evolutionary selective processes, Ala$_{51}$→Gly in the ginkgo tree[11] and Tyr$_{74}$→Phe in a thermophilic fungus *Humicola*[12]. The present sequence, along with that of *Crithidia*, is, however, outside that range, and according to the concept of Fitch and Markowitz might be expected to show variability in previously unvaried residues. This proves true as follows: *Euglena* Tyr$_{67}$→Phe, Ile$_{75}$→Val, and Lys$_{87}$→Ala (also *Physarum* (Lin, Niece and Fitch, unpublished)) *Euglena* and *Crithidia* Cys$_{14}$→Ala, Lys$_{27}$→Ser, Gly respectively; also the trivially unvaried position, 9 (only known previously in Saccharomyces, Ala) is Pro in *Crithidia*. These six, plus the two above, reduce the number of unvaried positions to 27. For this wider range of species the estimate of the invariable codons is reduced to 24±5, confirming the effect of species range.

Table 2 Properties of *Euglena gracilis* Cytochrome c 558

Molecular weight	
Gel filtration ('Sephadex G-75')	12,600±800
Sedimentation equilibrium ('Spinco' model E, 60,000 r.p.m. 20°)	10,940
Sequence analysis	11,254
Spectral characteristics	
Maxima (oxidized)	278, 365, 411, 530 nm
Maxima (reduced)	275, 320, 422, 525, 558 nm
mMolar extinction coefficient at 558 nm	25.7
Iso-electric point	9.55

The supposed invariability of several of the altered residues had been attributed to their presumed essential function. Cys$_{14}$ was considered necessary for the attachment of the haem. Its absence leaves an additional vinyl group conjugated with the haem system of double bonds and must be the major reason for the shift in the reduced maximum in the protozoan cytochrome to 558 nM. The two residues, Tyr$_{74}$ (*Humicola* Phe) and Ile$_{75}$ (here Val), are both part of a stretch of eleven consecutive residues not previously known to vary and considered part of a recognition site for other proteins[14]. Tyr$_{67}$ has been suggested to be involved in the passage of electrons in and out of the haem[15,16]. Much previous speculation must therefore be reconsidered in light of these findings.

Regarding the relationship between *Euglena*, *Crithidia*, and the metazoans, we conclude that the two protozoans are more closely related to each other than either are to the metazoans. This conclusion requires the examination of the messenger sequences of the proteins and the elimination of all non-critical positions. A non-critical position is a position for which the minimum number of nucleotide replacements required is independent of the phylogeny. For example, at codon 20, *Euglena* has alanine, *Crithidia* glycine, *Neurospora* glutamate, and pig, cotton and *Drosophila* all have valine. The central nucleotides of these codons must be C, G, A, U, U and U respectively. Because only one nucleotide appears more than once, then the minimal number of mutations is one less than the number of kinds of nucleotides regardless of the phylogeny assumed (4−1=3 in this position) and all mutations required by the data will be peculiar to the final leg descending to the exceptional taxon. Having eliminated the non-critical positions, we may then ask: what is the minimum pairwise distance (disjointness) between the species in the remaining critical

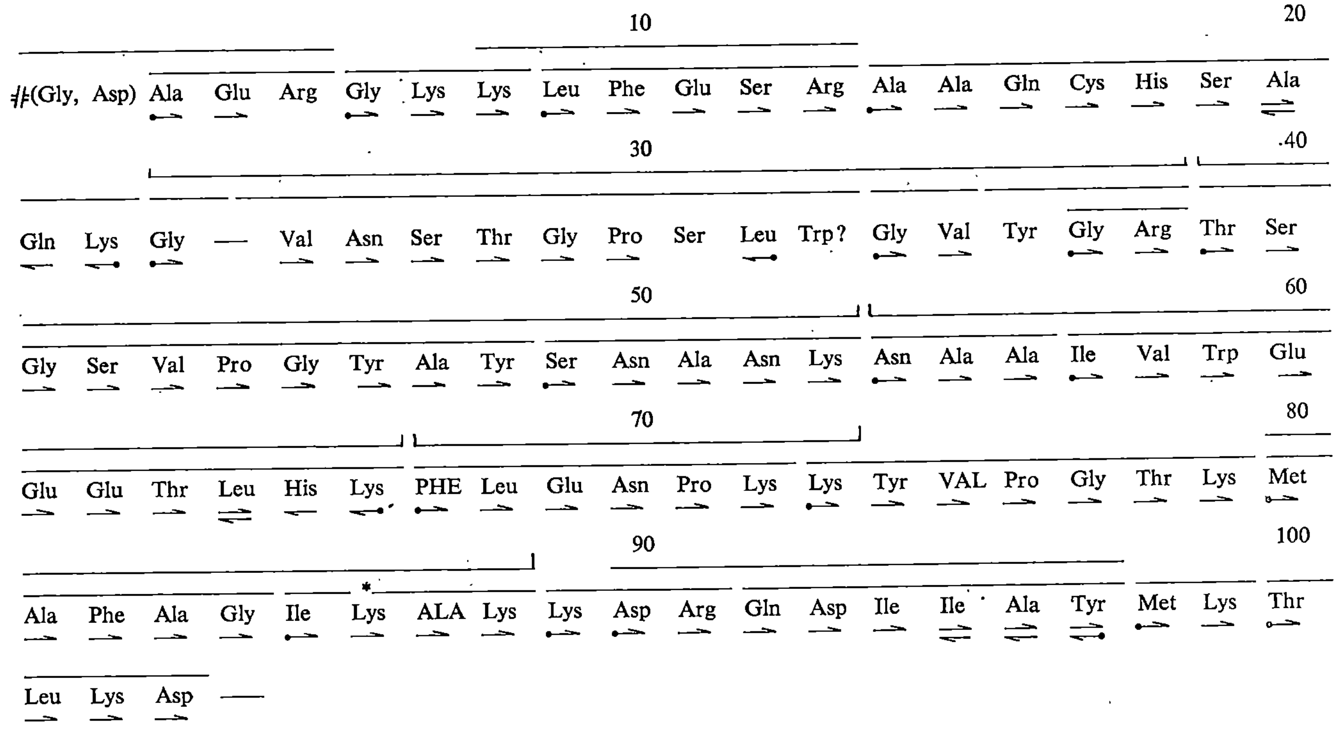
10
20
ac(Gly, Asp) Ala Glu Arg Gly Lys Lys Leu Phe Glu Ser Arg Ala Ala Gln Cys His Ser Ala
30
40
Gln Lys Gly — Val Asn Ser Thr Gly Pro Ser Leu Trp? Gly Val Tyr Gly Arg Thr Ser
50
60
Gly Ser Val Pro Gly Tyr Ala Tyr Ser Asn Ala Asn Lys Asn Ala Ala Ile Val Trp Glu
70
80
Glu Glu Thr Leu His Lys PHE Leu Glu Asn Pro Lys Lys Tyr VAL Pro Gly Thr Lys Met
90
100
*
Ala Phe Ala Gly Ile Lys ALA Lys Lys Asp Arg Gln Asp Ile Ile Ala Tyr Met Lys Thr
Leu Lys Asp —

Fig. 1 Amino-acid sequence of *Euglena gracilis* cytochrome c. The solid lines above indicate peptides isolated and sequenced. The solid lines with tick marks on their ends indicate peptides whose composition spans sequenced peptides. The ⇀ and ↼ arrows indicate residues determined by PTH-Edman and carboxypeptidase A or B procedures. The dot on the end of an arrow indicates that it is the first residue found by that procedure. The gaps at positions 24 and 104 are simply to show the alignment relative to other eukaryotic cytochromes c. The amino terminus (ac) is blocked, presumably by acetylation. Lys 86 (*) is trimethyl lysine. Position 33, (Trp?), was never identified directly, only spectrally and by Ehrlich reaction in this peptide. Positions previously unvaried (67, 75 and 87) are shown in capital letters. Tryptic digestion was carried out in 0.1 M NH_4HCO_3 for 5.5 h at 40° C with the cytochrome concentration at 1 % and TCPK-trypsin at 0.02%. The tryptic peptides were separated by *p*H gradient elution on 'Dowex AG-50W X_2' according to the method of Schroeder[5]. The tryptic peptides were repurified as necessary by paper chromatography. The amino-acid sequences of the peptides were determined by the method of Edman and Begg[6] as modified by Keresztes-Nagy, Perini and Margoliash[7]. PTH-derivatives were identified as fluorescence quenching spots after silica-gel chromatography in solvents IV and V of Jeppson and Sjöquist[8].

positions, that is, the only positions that, depending upon the phylogeny, could require parallel and back mutations? The results are shown in Table 3. Obviously, by eliminating substitutions peculiar to a single line, one tends to eliminate them most frequently from lines whose most recent ancestor common to the other taxa was longest ago. Thus "distance" is misleading and is the reason for using the term disjointness. It is clear that the two protozoans are less disjoint with respect to each other than either of them are to the metazoans. In this case, the number of possible unrooted phylogenies is only 105 and all 105 of them were tested and it was found that the fewest mutations were required in a phylogeny joining *Euglena* and *Crithidia*. A proper assessment of their relationship will better be made when additional protozoan sequences become available.

The work reported here was done independently of that of Pettigrew[13] with whom we agree as to the sequence of *Euglena gracilis* cytochrome c 558. It is our great pleasure to note the totally open communication with him since we became aware of our parallel pursuits. The assistance of Mr Frank Iltis and Dr George Tarr is recognized. This work was supported by a grant to W. M. F. from the US National Science Foundation.

Table 3 Minimum Pairwise Disjointness

		1	2	3	4	5	6
1	Pig	—					
2	*Drosophila*	17	—				
3	Cotton	39	43	—			
4	*Neurospora*	35	30	34	—		
5	*Euglena*	38	42	41	33	—	
6	*Crithidia*	43	38	33	34	26	—

The minimum pairwise disjointness is the number of nucleotides by which the mRNAs for cytochrome c from two species must differ in those nucleotide positions for which there are two or more different nucleotides appearing two or more times each. See text for explanation.

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Developmental Maturation of Susceptibility to Scrapie in Mice

AGE at the time of injection has not been shown to influence the incubation period of peripherally injected scrapie in mice over 6 days old[1], although a slight negative regression from birth to four months has been found for the intracerebral route[2]. We report here, marked incubation period changes of three scrapie agents given intraperitioneally when the mice were injected neonatally instead of as adults.

Table 1 The Incubation Periods Shown by Weanling Mice after an Intraperitoneal Injection of Various Strains of Scrapie Agent

Agent (mouse-passaged)	Inbred mouse strain	Dilution of infected brain	Incubation periods ± s.e. (days) in weanlings* Females	Males
22A	VM	10^{-2}	319±6	355±5
79A	VL	10^{-2}	205±1	215±2
ME7	C57BL	10^{-1}	225±4	233±3
		10^{-2}	249±2	250±4
		10^{-3}	278±6	275±3

* Weaned at 21 days old.

The inocula were 10^{-1}, 10^{-2} or 10^{-3} supernates (500 g, 10 min) of saline mouse-brain homogenates from terminal cases with ME7, 79A and 22A strains of scrapie[3-6]. Each agent was injected (0.02 ml.) intraperitoneally into C57BL, VL or VM mice, ranging in age from birth to 28 days. Any leakage of inoculum in 0 to 6 day old mice was minimized by inserting the fine needle (32G) anterior to the xiphisternum, through a long subcutaneous track, and penetrating the peritoneum adjacent to the liver, which assisted as a non-return valve. The injection site was sealed immediately with 'Nobecutane' acrylic solution. Table 1 gives incubation periods[4] for weanling mice with these agent/host strain combinations. Animals showing no clinical signs or histological lesions of scrapie, and which died or had to be killed over 550 days of age, were regarded as survivors. Depending on the particular agent/host combination, these survivors exceeded the mean incubation period for weanlings by more than 10 to 50 standard deviations.

Injection of very young mice frequently produced some survivors and a proportion of much longer or appreciably shorter incubation periods than those observed in weanling mice (Table 2). Cases following neonatal injection with ME7 agent tended to occur earlier with high titre inocula but later with low titre ones than in the weanling group, and survivors only occurred in the newborn group given the lowest titre. The proportion of survivors using 10^{-2} homogenates was higher with the 22A and 79A agents than with ME7. It must be emphasized that survivors do not occur in weanlings using these doses, either in these or in large numbers of other comparable experiments.

Several explanations for this phenomenon are relevant to the early pathogenesis of scrapie following peripheral inoculation. Neonatal mice probably lack some cell populations required for the initiation of pathogenesis. Hypotheses about the cause of the age-effect need to take account of the paradox that these data would give lower titre estimates using neonatal mice than using weanlings but with shorter incubation periods than weanlings at high doses. Two competing conditions may be present in the host, one favouring replication, the other destruction, of agent, and the outcome would depend on the balance of an individual's developmental state and the dose of agent.

The earliest replication of scrapie agent is known to take place in lymphoreticular tissue[7], indicating this to be the relevant system which is maturing in mice during the first postnatal week. There are numerous cell types in this tissue whose immaturity is involved in neonatal immunological immaturity[8,9] and age-dependent susceptibility to virus infections[10,11]. These age-dependent effects with scrapie are quite different from those with conventional viruses and, if due to lymphoreticular maturation, are unlikely to implicate either specific immune reactions or interferon production as these appear to play no part in the pathogenesis of scrapie[12-16].

The occurrence of survivors in mice given doses which would be lethal for all weanlings, raises the question of what happens to the agent in these individuals. There is no realistic possibility that leakage of inoculum can explain these results with the precautions we used, because even prolonged incubation periods would require the leakage of nearly all of it. The remarkable loss in effective titre, in conjunction with the

Table 2 The Distribution of Incubation Periods* of Three Scrapie Agents Injected i.p. in Mice of Different Ages

Agent (mouse-passaged)	Inbred mouse strain	Dilution of infected brain	Age (days)	Number of mice	Numbers of individuals with incubation periods in SD groups less than (−) or more than (+) the mean for weanlings. − > 3 SD	−3 to −2 SD	−2 to +2 SD	+2 to +3 SD	+ > 3 SD	Survivors†
22A	VM	10^{-2}	21–28	27	0	2	24	1	0	0
			4–6	16	2	0	9	1	1	3
			1	8	0	0	0	0	0	8
			0	10	1	0	0	0	0	9
79A	VL	10^{-2}	20–28	37	0	1	34	2	0	0
			6–7	28	0	6	15	5	2	0
			2–3	15	0	0	5	6	4	0
			0–1	24	1	1	0	2	11	9
ME7	C57BL	10^{-1}	21–28	8	0	1	7	0	0	0
			7–8	6	2	0	4	0	0	0
			0	17	7	3	2	0	5	0
		10^{-2}	21–28	20	0	0	19	1	0	0
			4–8	31	3	4	10	5	9	0
			2	7	1	3	2	1	0	0
			0–1	31	0	4	18	1	8	0
		10^{-3}	21–28	11	0	0	10	1	0	0
			8	8	0	0	2	1	5	0
			3	5	0	0	0	0	5	0
			0	6	1	0	0	1	2	2

* The individual incubation periods are classified in terms of standard deviations (SD) from the mean incubation period in weanling mice.

† Mice more than 550 days old, died or killed, with no signs of scrapie.

tentative conclusion that newborn mice lack one or more relevant sets of receptor cells, raises three possibilities for the fate of the agent. It could be removed either by excretion (for example, the neonatal gut is permeable at least to proteins), or by sequestration in tissues where it cannot replicate, do damage or gain access to target cells, or it could be inactivated enzymically, possibly by macrophages. Cases with very short incubation, in contrast, could result from high doses of agent overloading the hypothetical disposal systems, thus leaving some agent available when the receptors mature. This could be earlier in some individuals than others.

These experiments may explain maternal transmissions in sheep[17] and its absence in mice[18], because sheep are born with relatively more mature lymphoreticular responses[19]. This implies that the postulated receptors, though absent in newborn mice, are present in the sheep foetus.

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In vitro Morphine Antagonism by Antibodies

MORPHINE has a variety of pharmacological effects including inhibition of motility of some types of smooth muscle[1,2]. The narcotic antagonists nalorphine and naloxone appear to reverse a majority of the pharmacological effects of morphine by competitive inhibition for the tissue receptor site[1,2]. Our study was designed to determine if antibodies reactive with morphine could also inhibit or successfully reverse one of the biologic actions of the drug. We examined the capacity of rabbit antibodies produced by immunization with 6-succinyl-morphine conjugated to bovine serum albumin (M-6-HS-BSA)[3,4] to antagonize the depressant action of morphine on electrically-induced contractions of isolated guinea pig ileum.

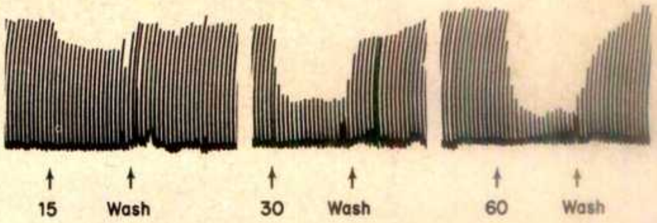

Fig. 1 Effect of 15 nM, 30 nM, and 60 nM morphine concentrations on the electrically-induced contractions of isolated guinea pig ileum. The amount of morphine added is expressed in terms of the final molar drug concentration in the bath that is 60 nM represents 0.6 nmol added to the 10 ml. bath. The drug was added to the muscle bath for 3 min periods and then washed out. There was an interval of at least 15 min between the addition of different drug concentrations.

A concentrated crude globulin fraction of hyperimmune serum obtained from a rabbit immunized with M-6-HS-BSA was prepared by precipitation with 50% ammonium sulfate followed by pressure dialysis. The reactivity of the antiserum has been studied in detail[5]. Concentrations of various opioids inhibiting binding of 88 pmol ml^{-1} of ^{14}C-morphine by 50% were; heroin, 0.10 nmol ml^{-1}; morphine, 0.11 nmol ml^{-1}; codeine, 0.16 nmol ml^{-1}; hydromorphine, 0.50 nmol ml^{-1}; nalorphine, 2.1 nmol ml^{-1}; meperidine, 80 nmol ml^{-1}; and naloxone, 30% inhibition at 1×10^3 nmol ml^{-1}. The concentrated globulin fraction bound 91,000 pmol morphine ml^{-1} as determined by the ammonium sulfate method[6,7] when the concentration of added antigen was 88 pmol ml^{-1} ^{14}C-morphine. Crude globulin from normal rabbit serum (NRS) and from rabbit antiserum reactive with BSA (anti-BSA) were prepared and concentrated by the same procedures. Specific binding of ^{14}C-morphine was not detected in either serum before or after ammonium sulfate fractionation. The protein concentration of each crude globulin fraction was adjusted to 30 mg ml^{-1}.

The assay for morphine activity was based on the depressant action of morphine on the electrically stimulated contractions of the longitudinal muscle of guinea pig ileum[8,9]. The ileal segment was stimulated coaxially with 1.5 times maximal rectangular pulses of 0.8 msec duration at a frequency of 6 pulses min^{-1}, and the muscle twitch was measured isometrically with an "E&M Model Six physiograph" and "Type A pressure transducer". There was an interval of at least 15 min between additions of different drug mixtures to the bath.

The inhibitory effect of increasing concentrations of morphine hydrochloride on the muscle twitch is shown in Fig. 1. The drug was allowed to remain in the bath for 3 min and then washed out. Inhibition was observed immediately upon addition of morphine to the bath and this inhibition was reversed on removal of the drug by washing. The lowest concentration at which this effect could be detected was at 15 nM morphine. Inhibition was 70–80% complete at 60 nM morphine concentration.

The capacity of anti-M-6-HS-BSA to antagonize the depressent actions of morphine on the ileal segments was measured. Varying concentrations of morphine were preincubated with 0.4 ml. of antibody globulin for 15 min at room temperature, and then added to the tissue bath for 3 min. This amount of antibody inhibited the effect of morphine concentrations ranging from 60 nM to 1,000 nM (Fig. 2). Morphine preincubated with NRS globulin retained full activity, and addition of antibody or NRS globulin alone had no effect on the contractility of the ileal muscle. This prevention of the pharmacological effect of morphine on isolated guinea pig ileum was probably due to the morphine-antibody combination stopping the morphine reaching the biological receptor sites. Prevention of the morphine effect was complete when a two-fold stoichiometric excess of antibodies was present.

To determine if antibody was able to reverse morphine

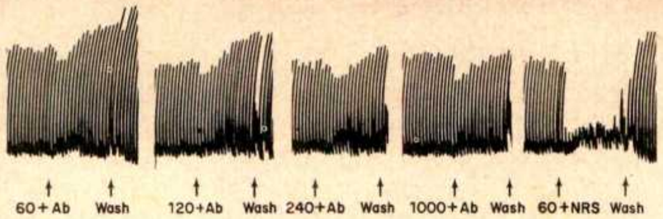

Fig. 2 Effect on the electrically-induced contractions of isolated guinea pig ileum of adding 0.4 ml. anti-M-6-HS-BSA globulin (Ab) preincubated with either 60 nM, 120 nM, or 1,000 nM morphine; and the effect of adding 0.4 ml. normal rabbit globulin (NRS) preincubated with 60 nM morphine.

action, antibody was added to the muscle bath 1 min after addition of morphine when the induced inhibition of muscle contraction was maximal. Typical results are illustrated in Fig. 3*a*. Anti-M-6-HS-BSA added for 1 min after morphine completely reversed the inhibition of muscle twitch caused by 120 nM morphine. The recovery of the twitch response was complete within 2 min and this effect appeared to be identical to that observed after addition of 10 nM naloxone. (Fig. 3*b*). Neither NRS globulin or anti-BSA globulin (Fig. 3*c*) had any effect on the morphine-induced inhibition of the muscle twitch. Reversal of the morphine effect was about 80% complete when a stoichiometrically equivalent amount of antibody was added to the muscle bath.

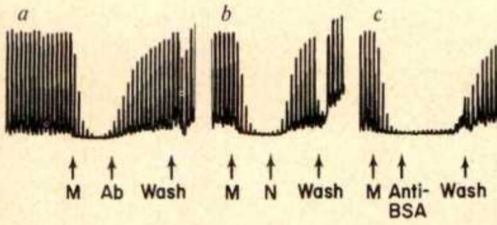

Fig. 3 Effect on the electrically-induced contractions of isolated guinea pig ileum of 120 nM morphine (M) present in the muscle bath for 1 min followed by the addition of either: *a*, 0.5 ml. of anti-M-6-HS-BSA (Ab); *b*, 10 nM naloxone (N); or *c*, 0.5 ml. of anti-BSA.

Similar experiments have been carried out with globulin obtained from several rabbits immunized with morphine-6-succinyl-BSA, with identical results. We suggest that because anti-BSA globulin has no effect on the morphine activity the inhibition of biological action of morphine is the specific effect of antibodies reactive with morphine.

Results of our experiments indicate that sepecific antibodies are capable of antagonizing the inhibitory effect of morphine on the electrically stimulated contractions of guinea pig ileum. The antibody molecules apparently bind morphine more strongly than the tissue receptor site as antibodies were able to prevent and reverse the inhibitory effect of morphine on smooth muscle contraction. The use of this sensitive *in vitro* assay together with immunochemical measures of antibody avidity should allow determination of the molar concentrations of antibody required for morphine antagonism and the relative affinities of morphine receptors in tissues for their drug substrates.

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Glucose Catabolism by the Simian Malaria Parasite ***Plasmodium knowlesi***

ALTHOUGH the parasitology of malaria has been extensively studied[1], biochemical aspects of the relationships between the intra-erythrocytic parasite and its host erythrocyte are poorly understood. The main source of metabolic energy for the erythrocytic stages of the parasite is the breakdown of glucose with formation of lactic acid[2–6], which it may carry out independently of the red cell[2]. Catabolism of glucose by metabolic pathways other than glycolysis may occur, although the overall pattern of glucose breakdown appears to vary with the species of malaria parasite[7]. The ability of the parasite, as distinct from the erythrocyte, to carry out the reactions of the pentose phosphate pathway is unresolved[8–11,19].

Here we have attempted to estimate the flux of glucose through the glycolytic pathway, in normal rhesus monkey erythrocytes, in erythrocytes infected with *P. knowlesi* and in parasites "freed" from their host erythrocytes. *P. knowlesi* shows synchronous growth with a 24 h asexual life cycle and parasites may therefore be conveniently prepared from the monkey host in relatively large quantities at well defined life

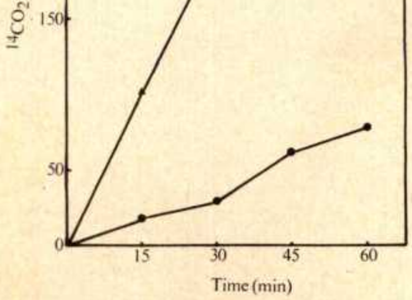

Fig. 1 Production of $^{14}CO_2$ from 1-^{14}C- and 6-^{14}C-D-glucose in erythrocytes of the rhesus monkey infected with *Plasmodium knowlesi*. ▲, 1-^{14}C-D-glucose; ●, 6-^{14}C-D-glucose.

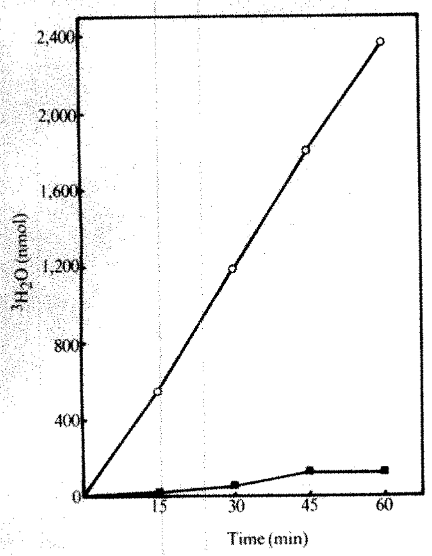

Fig. 2 Release of ^3H_2O from 2-^{3}H-D-glucose by erythrocytes from the rhesus monkey. ■, Normal; ○, infected with *Plasmodium knowlesi*.

cycle stages. Parasites were prepared when they had grown to the late trophozoite and schizont stages.

The flux of glucose through the glycolytic pathway and the primary dehydrogenases of the pentose phosphate pathway was measured radiochemically by the method of Hutton[12] which estimates glycolytic flux as the release of ^3H_2O from 2-^{3}H-D-glucose in the hexosephosphate isomerase (EC 5.3.1.9) reaction. Flux through the primary dehydrogenases of the pentose phosphate pathway was estimated from the release of $^{14}CO_2$ from 1-^{14}C-D-glucose and 6-^{14}C-D-glucose.

The results (Figs. 1 and 2) show that the release of ^3H_2O from 2-^{3}-H-D-glucose and of $^{14}CO_2$ from 1-^{14}C- and 6-^{14}C-D-glucose were linear over the experimental time. The flux of the glucose through the glycolytic pathway obtained by radiochemical investigation agreed with the values obtained by measuring production of lactic acid, and was greatly increased in the parasitized erythrocytes as compared with normal erythrocytes (Table 1). A high value for glycolytic flux was observed in the free parasites.

The results presented in Table 1 show also that the flux of glucose through the primary dehydrogenases of the pentose phosphate pathway was very much greater in parasitized erythrocytes than in normal erythrocytes. This large increase in metabolic activity was retained with the parasite when "freed" from its host erythrocyte.

The high $^{14}CO_2$ production from 6-^{14}C-D-glucose indicated the presence of an oxidative metabolic process in the parasitized erythrocyte and in the "free" parasite preparation. This value is higher than can be accounted for by recycling through the hexose phosphate pool[16,17]. Randomization of the C_6 position into the C_1 position of the hexose phosphate pool indicates that the specific activity of the C_1 position may be up to 20% of the initial specific activity of the C_6 position[18]. A reasonable estimate of the maximal rate of $^{14}CO_2$ production from 6-^{14}C-D-glucose recycling through the pentose phosphate pathway would be about 20% of the rate of $^{14}CO_2$ production from 1-^{14}C-D-glucose assuming 100% recycling. Observed values would probably be lower than 20%. Although extensive recycling of hexose phosphate in the erythrocyte has been reported[20] it is most unlikely that 100% of the hexose phosphate produced in the pentose phosphate pathway would be recycled by glucose-6-phosphate. Our results show that the rate of production of $^{14}CO_2$ in the parasitized erythrocyte was between 19–28% of the rate of production of $^{14}CO_2$ from 1-^{14}C-D-glucose. In the "free" parasite preparation the corresponding figure lay between 22% and 50%. This suggested that $^{14}CO_2$ was produced from 6-^{14}C-D-glucose by processes other than recycling through the pentose phosphate pathway.

We believe that our results represent a valid assessment of the flux through the glycolytic pathway and through the primary dehydrogenases of the pentose phosphate pathway, though the method yields no information of the fate of end products and intermediates of these pathways. Glycolytic flux is measured as the flux through the first enzyme peculiar to the glycolytic pathway. It is an accurate measurement of the flux of glucose through to pyruvate only if the pentose phosphate pathway is of small activity compared to the glycolytic activity. In our system, 20% or less, of the glucose appears to be metabolized by the initial enzymes of the pentose phosphate pathway. We consider that this, together with the agreement between radiochemical measurements of the glycolytic flux and measurement of lactate production provides good evidence that the radiochemical measurement is giving an acceptable assessment of glycolysis and that the method is a valuable tool for the investigation of metabolic characteristics in malaria infection.

Our results show therefore that the breakdown of glucose in the parasitized erythrocyte, by both glycolysis and the pentose

Table 1 Glycolytic Flux and Lactate Production

	^3H_2O release nmol/10^9 cells h^{-1}	Lactate production nmol/10^9 cells h^{-1}	$^{14}CO_2$ production from: 1-^{14}C-D-glucose nmol/10^9 cells h^{-1}	6-^{14}C-D-glucose nmol/10^9 cell h^{-1}
Normal erythrocytes	75– 155 (4)	180– 224 (4)	9– 16 (3)	Not detected
Parasitized erythrocytes	800–2,360 (3)	1,988–4,912 (5)	348–410 (3)	67–116 (3)
"Free" parasites	1,080–3,600 (3)	None available	368–478 (3)	78–196 (3)

Values given are upper and lower values in the observed range. Number of experiments is shown in parentheses. Both parasitized erythrocytes and free parasites for the radiochemical experiment were prepared from blood from the same infected rhesus monkey. Erythrocytes were prepared from freshly drawn heparinized blood by centrifugation at 1500*g* for 10 min, washed twice under the same conditions in Krebs glucose saline, and separated from white cells and platelets using a sucrose gradient[13]. Parasites were freed from host erythrocytes by immune lysis[14]. Erythrocytes and parasites were washed three times by centrifugation at 1500*g* for 10 min with the medium used in the glycolytic incubation[15]. Erythrocytes and parasites were finally suspended in the glycolytic medium to 50% haematocrit. The cells were incubated in closed Warburg flasks containing: 2.0 ml. glycolytic medium, 0.5 ml. erythrocyte or parasite suspension with 0.5 µCi 1-^{14}C or 6-^{14}C-D-glucose and 1.5 µCi 2-^{3}H-D-glucose. The reaction was terminated by tipping 0.5 ml. of 20% TCA from the side arm and carbon dioxide evolved was trapped in 0.3 ml. hyamine (Koch–Light Labs, Bucks) in the centre well. The flasks were pre-incubated 15 min at 37° C before addition of the radioactive substrate in 10 µmol of carrier glucose. At the end of the experiment the flasks were further shaken in the 'New Brunswick Controlled Environment Incubator' for 1 h at 50 to 60 cycles per min to remove final traces of $^{14}CO_2$. Recovery of $^{14}CO_2$ was calculated by trapping $^{14}CO_2$ evolved from a known addition of $Na_2{}^{14}CO_3$ after the addition of TCA. This was estimated as 70±2%. ^3H_2O was sublimed from the incubation mixture under vacuum in Thunberg tubes, trapping the sublimed ^3H_2O by immersing one end of the tube in a dry-ice-methanol bath. Counting of the $^{14}CO_2$ was performed in toluene based scintillator (6 g PPO, 0.12 g POPOP $l.^{-1}$) and the ^3H_2O was counted in a Dioxan based scintillator (180 g $l.^{-1}$ naphthalene 4 g PPO, 0.1 g POPOP $l.^{-1}$). All counting was performed on a 'Packard liquid scintillator spectrometer'. Erythrocyte and parasites were counted using a 'Thoma' haemocytometer with Neubauer ruling after dispersing parasites by drawing through a syringe needle several times.

phosphate pathway, was very much increased compared with the normal erythrocyte. These activities were recovered, at least in part, with the parasite when it was "freed" from its host erythrocyte. We have not made a quantitative assessment of this recovery, nor does this observation indicate that the activity observed is of parasite origin. The immune lysis method used to "free" the parasites may not remove the erythrocyte membrane from the parasite-erythrocyte complex although the host cell haemoglobin was removed, and it is possible that host erythrocyte glycolytic enzymes may be retained in the "free" parasite preparation associated with this[21–23]. It is essential to discover from the point of view of the host-parasite relationship, if the increase in metabolic activity is due to the elaboration of an independent metabolic capability by the parasite, or if the parasite can enhance and utilize the metabolic processes of its host erythrocyte.

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A Preliminary Investigation of the Swine Vesicular Disease Epidemic in Britain

ON December 11, 1972, an outbreak of vesicular disease in pigs was reported from Staffordshire. It was diagnosed as foot-and-mouth disease (FMD) on clinical grounds but this was not confirmed on initial serological tests. Investigations were carried out to determine the nature of the aetiological agent.

Outbreaks of disease have occurred in pigs on two previous occasions which have been clinically indistinguishable from FMD, but from which different causal agents have been isolated. Nardelli *el al.*[1] desbcribed such a syndrome in Italy in 1966, and suggested that the agent responsible was a porcine enterovirus, and this has been confirmed by Newman *et al.*[2]. Another outbreak in pigs in Hong Kong in 1971 was reported by Mowat *et al.*[3] and the causative agent was again described as a porcine enterovirus (Hong Kong 1971), serologically similar to the Italian enterovirus.

The disease as observed in Britain closely resembles that described in these two reports (A. J. G. Stubbins, R. S. Hedger and G. N. Mowat, personal communication). It occurred only in pigs although on several premises cattle or sheep were in close contact with large numbers of the infected animals. Fifteen outbreaks were confirmed in four weeks, eight being in the first week. Several outbreaks occurred in pigs which were fed on swill collected from the Birmingham area, and in a number of instances spread from the first reported outbreak could be attributed to the movement of pigs or of people. The pattern of disease spread suggested an incubation period of four to six days. Morbidity rates of up to 60% were recorded and the lesions could not be differentiated from those of FMD.

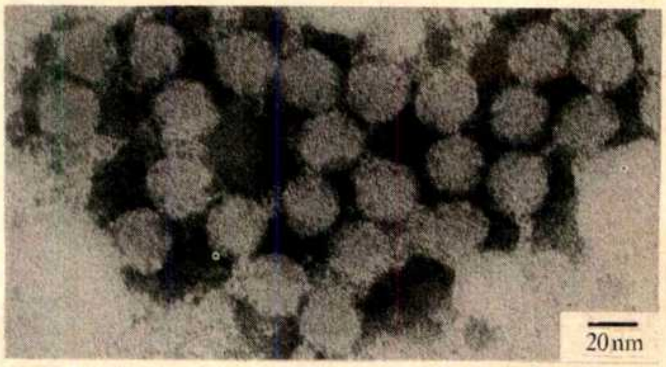

Fig. 1 Electron micrograph of complexes of the swine vesicular disease virus (England 1972) with antiserum to the Hong Kong 1971 enterovirus.

Vesicular fluid, extracts of vesicular epithelium and fluid from infected tissue culture monolayers were tested by complement fixation for the presence of FMD virus or enterovirus antigens. Hyperimmune guinea-pig sera were used which had been prepared against all seven types of FMD virus and against the Italy 1966 enterovirus. The tests were performed in microplates using a fixed complement dose of five 50% haemolytic units and a constant amount of antigen. The antisera were diluted in 1.5-fold series from starting dilutions of 1/16; plates were incubated for 18 h at 4° C. In all of the samples tested there was no reaction with any of the FMD virus antisera. Positive results, however, were obtained with the Italy 1966 enterovirus antiserum, in many instances using material from infected pigs and in all tests in which tissue culture fluid was used from monolayers showing extensive cytopathogenic effects.

To further verify the identity of the virus, virus from infected tissue culture fluid was purified, mixed with serum from a pig convalescent from Hong Kong 1971 enterovirus and examined in the electron microscope ('Siemens Elmiskop I'). Complexes of virus and antibody were seen (Fig. 1), which were also present in mixtures of virus and the Italy 1966 enterovirus antiserum, but were not observed when the virus was mixed with FMD antiserum.

FMD virus differs from enteroviruses in being acid-labile, exposure to *p*H 5 causing a reduction in infectivity by degradation of the virion to its RNA and protein subunits[4]. Swine vesicular disease virus (England 1972) when so treated showed no loss of infectivity (J. N. Wilson, personal communication), and electron microscopy showed that after acid treatment, no virions were observed in FMD virus samples but in samples of swine vesicular disease virus the virions remained intact (Fig. 2).

Cell monolayers of primary calf thyroid and BHK 21 tissue cultures inoculated with extracts of vesicular epithelium showed minimal cytopathogenic changes and although virus was isolated from them after 48 h, direct evidence of replication has not yet been obtained. Twenty-four h slope tube cultures of the pig kidney cell line IB-RS-2, inoculated with the same material, showed plaques of round, refractile cells 24 h after infection, which progressed to a total destruction of the cell sheet after 48 h. Virus adapted by serial passage to IB-RS-2 cells grew to titres of up to 2×10^9 p.f.u. per ml. of tissue culture fluid. Primary pig kidney cell monolayers were less susceptible than IB-RS-2, but there was cytopathic effect and virus multiplication.

The presence of the virus in tissue cultures showing typical cytopathic effect was confirmed by complement fixation tests. This cytopathic effect was inhibited by antisera to the Italy 1966 or Hong Kong 1971 enteroviruses.

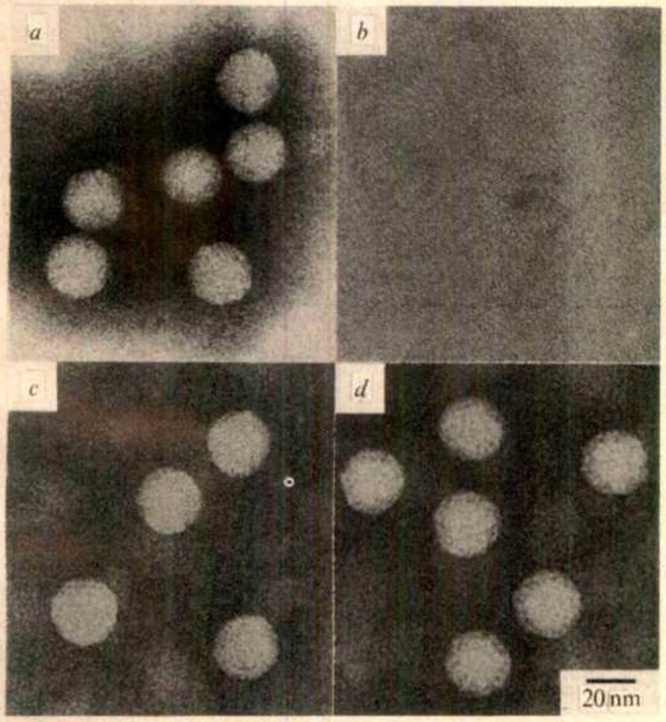

Fig. 2 Electron micrographs of FMD virus and swine vesicular disease virus before and after treatment with carbon dioxide. Droplets containing virus were placed on electron microscope grids and exposed to either moist CO_2 gas or moist air for up to 10 min. After draining they were stained with phosphotungstic acid at *p*H 7.2. — *a*, FMD virus; *b*, FMD virus plus CO_2; *c*, swine vesicular disease virus; *d*, swine vesicular disease virus plus CO_2.

Rabbits inoculated intravenously, and guinea-pigs intradermally in the plantar pads with the 1972 England virus showed no evidence of virus multiplication or of lesions. I.p. inoculation of 6-day-old mice with $10^{4.5}$ TCID_{50} of virus however caused paralysis and death between 3 and 8 days after inoculation.

Samples of vesicular fluid and an extract of vesicular epithelium from two field cases were each inoculated intradermally into the tongue of one steer and the bulbs of the heels of two pigs. No lesions were observed in the cattle, but in the pigs, lesions became apparent after 24 h when there was blanching of the epithelium around a number of the inoculation sites. After a further 12 h, vesicles had appeared on the heel bulbs and later all feet became involved with further vesicles developing in the interdigital area and around the coronary bands of the primary and accessory digits (Fig. 3). Vesicles and erosions were observed on the lips, gums and tongue of some pigs, and fever (up to 42° C) was noted. Samples of vesicular epithelium from the pigs, tested by complement fixation, gave positive results with the Italy 1966 enterovirus antiserum and yielded up to $10^{7.6}$ TCID_{50} of virus per gram of epithelium when titrated on IB-RS-2 cell monolayers.

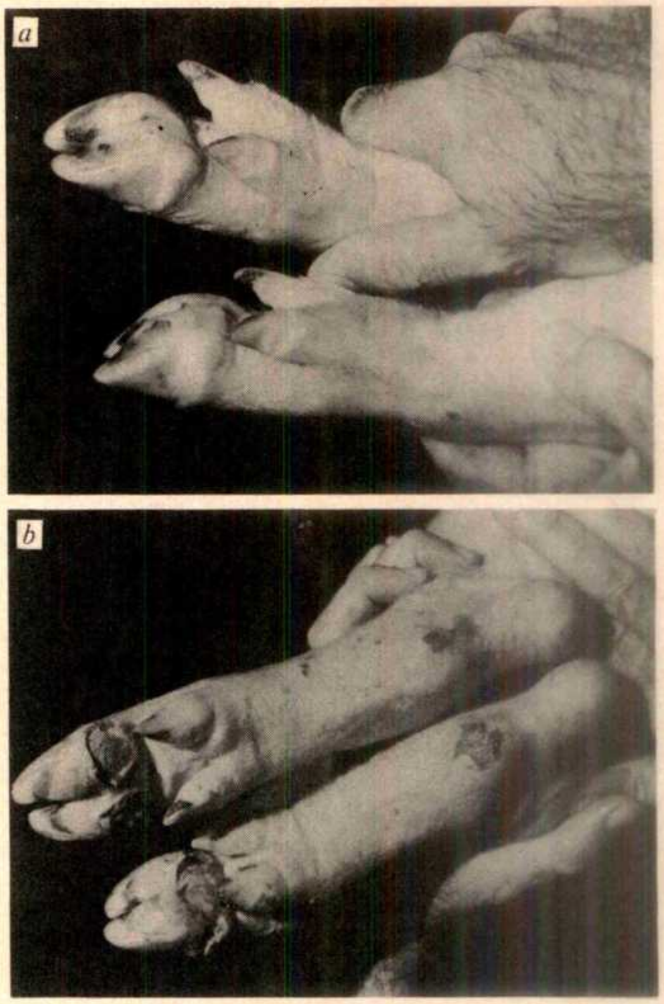

Fig. 3 Feet of pigs infected with the swine vesicular disease virus (England 1972) showing lesions (*a*) 1 day old and (*b*) 8 days old.

Two days after inoculation of the four pigs, a further eight were placed in contact with them. All developed generalized disease of a similar description after 2 to 6 days and neutralizing antibody to the England 1972 virus was demonstrable in their serum after 4 days (R. S. Hedger, personal communication).

It seems that the causative agent of these first recorded British outbreaks of swine vesicular disease is a porcine enterovirus, serologically similar to those responsible for the Italian and Hong Kong outbreaks. The generally slower spread and lower morbidity observed in the field, when compared with FMD, may be explained by a lower output of virus from infected pigs. To obtain an estimate of the virus content of the animals' environment, pens containing infected pigs were sampled for the presence of virus. Slurry collected from the floor yielded up to 10 TCID_{50} per ml. during the period that pigs showed clinical lesions. Air sampled by collecting swabs of nasal mucus from personnel working in the pens during the same period contained no recoverable virus. These results suggest that the amount of viral excretion from the pigs was considerably less than would occur with pigs infected with

FMD, and further work is in progress to investigate methods of spread.

The origin of the virus is at present subject to speculation. There are recent reports from Europe of several similar outbreaks in pigs. Samples from infected pigs sent to Pirbright from outbreaks in two other countries have been tested by complement fixation and given positive results with the Italy 1966 antiserum. Further work is being carried out to establish the serological relationship of the England 1972 virus to porcine enteroviruses isolated from concurrent and past outbreaks of vesicular disease in pigs.

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Evidence for an Empty Core in a Bacterial Flagellum

BACTERIAL flagella have three parts; a basal structure which is attached to the plasma membrane, a hook-like structure and a long filament which is outside the cell envelope. Flagellar filaments have been extensively studied[1] and have been shown to be composed of an array of flagellin subunits. Various models have been proposed for the arrangement of the subunits in the flagellum, a common feature of which is a helical array with a hollow central core. Evidence for such a core has only rarely been obtained in electron micrographs of negatively-stained flagella when the flagella are still attached to the bacterium[2], although in the proposed models the core is sufficiently large to allow easy penetration of negative-staining solutions.

Flagellar filaments grow at the end distal to the bacterium, and flagellin is synthesized on ribosomes within the cell; these observations therefore raise the question of how the flagellin molecules are transported to the site of assembly. Kerridge[1] considered that it is most improbable that flagellin molecules are excreted into the growth medium for subsequent assembly onto flagellar filaments, or that they travel along the outside of the flagellum, and concluded that the molecules enter the basal structure and then travel through the centre of the filament to the distal end. If this is correct, it would explain why negative staining solutions are unable to penetrate into the core of the flagellum, as the core would be blocked by flagellin molecules. There is no direct evidence, however, for the presence of free flagellin within the flagellum.

We were therefore interested to see apparently empty cores in flagella in freeze-etched preparations. Frozen cultures of the hyperthermophilic bacterium, *Clostridium thermohydrosulfuricum*, strain L77[3], in the late logarithmic phase of growth, were fractured at −196° C[4,5]. Figs. 1 to 3 illustrate flagella lying on the surface layer of the cell wall which is composed of a hexagonal array of subunits.

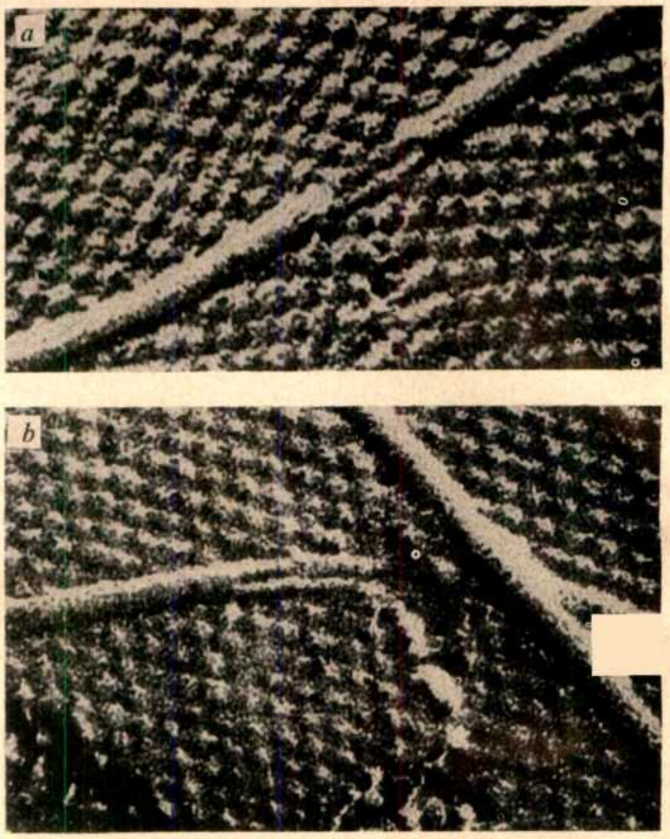

Fig. 1 *a* and *b*, Flagella about 15 nm in diameter lying on the surface of the cell wall. The regular array of subunits on the cell wall is partly destroyed near the fractured regions of the flagella. ×120,000.

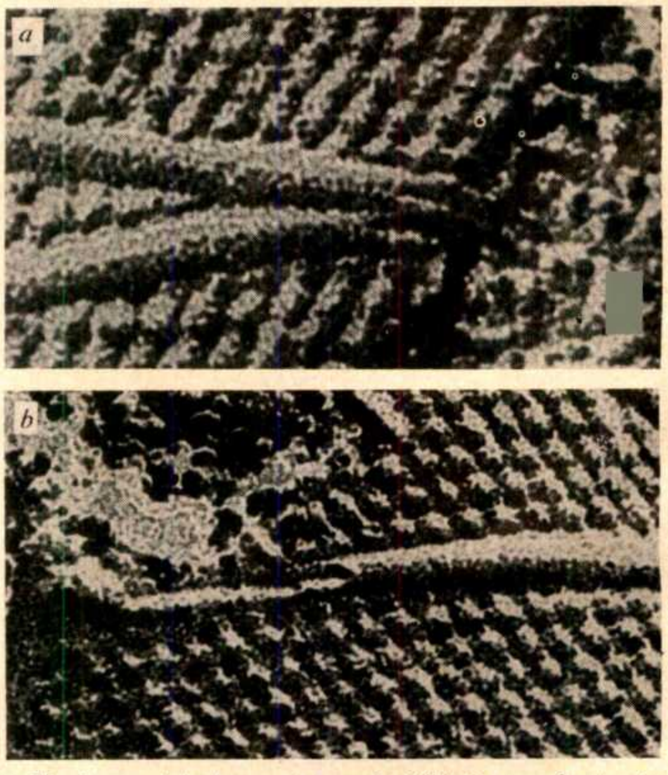

Fig. 2 *a* and *b*, An empty core is visible in cross-fractured flagella in regions where the cell wall and cytoplasmic membrane have also been split away. *a*, ×200,000; *b*, ×140,000.

Different fracture planes are seen in the flagella, and in some regions part of the flagellum has broken away to reveal an empty core. An examination of the micrographs makes it clear that these cores are revealed by the freeze-fracturing and etching process, and are not errors in flagella synthesis. Near

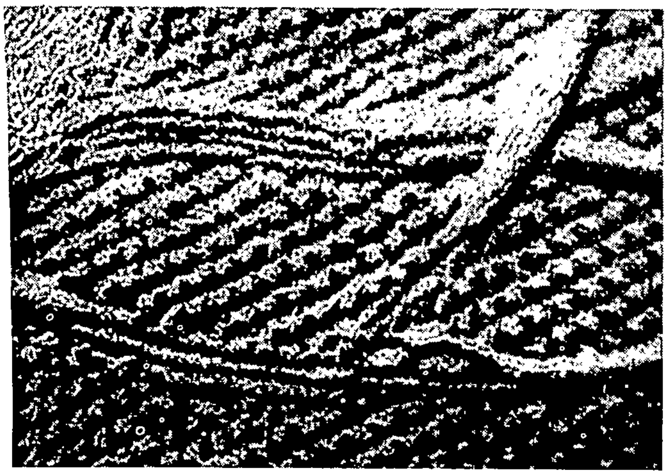

Fig. 3 A group of flagella, two of which are lying parallel to each other, all show longitudinal fractures and hollow cores. ×120,000.

the sites along the flagella, where the core is visible, the regular pattern on the surface of the cell wall is sometimes partly destroyed (Fig. 1*a* and *b*) indicating that these are regions of fracture. The majority of the flagella which show the cores are fractured in regions in which parts of the wall and cytoplasmic membrane have also been split away (Fig. 2*a* and *b*). The fact that the fractured flagella always appear as hollow half-cylinders is evidence that they were originally filled with etchable material. If densely-packed flagellin molecules had been present there would be an equal probability that they would either remain within the fractured regions and be seen protruding from the half-cylinders, or be removed with the half of the flagellum. Complete confirmation of this can be obtained by the study of complementary fracture faces[4].

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Alpha Rhythms and Hyperkinesis

IN his comment on my report "Alpha Rhythms in the Hyperkinetic Child"[1], Davidson[2] stated that my data support Lippold's hypothesis[3] that "Oscillation in striate muscle control systems is the source of alpha rhythm". He quoted the work of Mulholland and Evans[4,5] which suggested that presence or absence of alpha rhythms was not determined by the presence or absence of relaxed wakefulness, but by oculomotor function. Many arguments have been presented against such a hypothesis[6-9], Butler and Glass[10] have presented findings inconsistent in a number of respects with the view of ocular tremor as a generator of alpha rhythm, and suggested that eye movements in their turn may be modulated by alpha rhythms when conscious control of fixation waned or was interrupted by eye closure. Chapman *et al.*[11] repeated the basic experiments of Mulholland and Evans[4,5], taking care to eliminate effects of differential visual input, and demonstrated that alpha activity was influenced by visual input and not by eye position.

Contrary to what Davidson states[2], the article by Darrow *et al.*[12] does present data from a simplistic experiment showing that alpha returns with "automation" or habituation to a stimulus. Dempsey and Morrison's[13] concept of a sub-cortical thalamic pacemaker, Jasper's[14] work describing an intrathalamic pacemaking system, the theory of Andersen and Andersson involving recurrent inhibitory systems in the thalamus and the relation of all these to human alpha rhythms has been reviewed by Andersen and Andersson[15]. Barlow and Estrin[16] have recently presented evidence which suggested that alpha activity represented summated polysynaptic potentials under thalamocortical control.

Habituation of the alpha attenuation response has been studied in hyperkinetic children, and exaggerated initial response to novel stimuli and decreased capacity to disattend to redundant events has been demonstrated[17]. In a study of the alpha average, greater spread of frequency abnormalities and poor spatial organization has also been shown in such children[18]. In a current prospective study I have observed that about 60% of hyperkinetic children do not have well organized alpha rhythms in amounts appropriate for their age. Preliminary observations seem to indicate that with increasing age and decreasing hyperkinesis, alpha activity shows proportionate increase in amount and organization in these children. These observations in addition to the literature cited above lend some support to the contention that alpha rhythm in the human EEG is an index of relaxed wakefulness.

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Amino-acids in Nectar and their Evolutionary Significance

IT has been known since ancient times that nectar, usually secreted from specialized glands within flowers, is utilized by anthophilous (flower-visiting) animals for the energy-providing sugars that it contains. It is usually assumed that protein-making materials will be obtained elsewhere, from larval feeding (Lepidoptera), from pollen (Hymenoptera—Apioideae) or (by vertebrates) from insects. However, some butterflies are known to be attracted to decaying flesh, faeces, urine and stagnant water[1] and well as sweat[2], while many take phloem-sap from a wound or honey-dew excreted by aphids[1]. Moths are known to drink fruit juices, sweat, secretions from the eyes of animals, and even mammalian blood[3]. Unusual feeding-behaviour is shown by butterflies of the genus *Heliconius* which collect pollen, steep it in nectar, and subsequently ingest the amino-acids that diffuse from the grains[4].

This evidence of concern with amino-acid ingestion by adult insects usually thought of as restricted to a liquid diet suggests that nectar itself should be examined as a potential source. Some comprehensive analyses of honey (which contains additives provided by its makers, the honey bees), have revealed the presence of substances other than carbohydrates[6–10], but analyses of nectar[11,12] appear to have been virtually restricted to studies of the amounts and proportions of the sugars present. Consequently, a survey of 266 species of flowering plant occurring in nature in California and in the University of California Botanical Gardens has been made. The results show that the occurrence of significant concentrations of amino-acids in nectar is the rule.

Nectar was taken from flowers at the time of maximum production, usually mid-morning, using a fine capillary tube, taking precautions to avoid any contamination by pollen. Nectar drops placed on filter-paper were allowed to dry and then stained with ninhydrin (0.2% in acetone) and up to 24 h at laboratory temperature allowed for the usually violet colour to come to a maximum. A comparison scale for colour depth was created by making dilutions of an aqueous solution of histidine and staining these (1=49 μM; 2=98 μM; .....; 10=25 mM). Each sample was scored again this linear "histidine scale". Proteins (tested electrophoretically in several samples) seem not to be present in quantities significant for animal nutrition.

Table 1 Amino-acid Concentration of Nectar in Flowers of Different Pollination Type

Flower pollination type	No. of species	Mean (on histidine scale)	Range	Coefficient of variation (%)
Bee	95	4.76	0–9	47
Butterfly and bee	44	6.02	3–8	23
Butterfly	41	6.68	4–10	21
Moth	30	5.60	0–9	45
Bird	49	5.22	1–9	37
Fly (unspecialized)	34	3.77	0–9	57
Fly (specialized)	8	9.25	7–10	—

A summary of results on a pollination type basis is given in Table 1. The nectar richest in amino-acids is that which is produced in small quantity by flowers that by their appearance and smell attract carrion- and dung-flies away from their usual sources of nutrients. Nectars produced rather copiously by flowers which are primarily visited by butterflies are also consistently rich in amino-acids, slightly more so, on the average, than those from flowers visited freely by both butterflies and bees. Judging by their mean score on the "histidine scale" (6.68), about 0.3 ml. of "butterfly flower" nectars would contain about 840 nmol of amino-acids. This is the quantity of free amino-acids that Gilbert[4] believes would be obtained from a day's harvest of pollen (1.5 mg) by the uniquely pollen-collecting *Heliconius* butterflies (apparently producing a profound effect on their life-span and reproductive output). 0.3 ml. of nectar could be provided by no more than fifteen flowers of *Dianthus barbatus*, and some "butterfly flowers" produce more than this species. Consequently, nectar cannot be ignored as a potential source of amino-acids for the nutrition of butterflies as well as carrion- and dung-flies.

On average, the amino-acid concentration in the nectars of flowers visited by bees is significantly lower than that of "butterfly flowers", even though less is generally produced. Values range from 0 to 9 on the "histidine scale". These results suggest that for bees, which have a rich alternative source of proteinaceous materials in pollen, the amino-acids in nectar are less important than they are for butterflies. An even lower mean is shown by "unspecialized fly flowers" that expose their nectar freely to syrphids and other diptera (as well as bees and beetles) that also taken pollen as food. In 1873 Hermann Müller[5] described and interpreted correctly the behaviour of the dipteran *Rhingia rostrata* taking both nectar and pollen from the same flower of *Lythrum salicaria*.

For moths, there is also a wide range of amino-acid concentrations in the nectars of the flowers they prefer. The same is true of "bird flowers" (where a rather low mean is explicable on the basis of the birds' utilization of an alternative protein source in insects).

Flowering plants belonging to some taxa notable for "primitive" characters (such as *Drimys winteri, Liriodendron tulipifera*, members of the Ranunculaceae, and some palms) contain some amino-acids in their nectar. Consequently, it may be supposed that amino-acids have been a constituent of flowering-plant nectars since the early stages of their evolution. Nevertheless, there is evidence that, as the evolution of specialized pollination systems has proceeded, selection has taken place for consistent high concentrations of amino-acids. No satisfactory linear phylogenetic arrangement of flowering plant families exists; nevertheless data from the available taxa may be subjected to a series of comparisons based on their possession of what are generally considered "primitive" or "advanced" characters, taken one at a time (Table 2). Consistently, the means for plants showing the "advanced" character are higher (while the coefficient of variation is smaller). However, there are differences with a direct taxonomic basis; high values were given by the tested members of such families as the Asclepiadaceae, Liliaceae, Campanulaceae and Leguminosae, while notably low values characterize the tested members of the Myrtaceae, Caprifoliaceae and Saxifragaceae. The Rosaceae shows a wide range of values.

Table 2 Amino-acid Concentration in Nectar in Different Flower Types

	No. of species	Mean (on histidine scale)	Coefficient of variation (%)	*P**
Polypetalous	105	4.75	45	≪0.001
Sympetalous	161	5.90	34	
Actinomorphic	158	5.15	42	=0.001
Bilateral	108	5.99	34	
Exposed nectar	73	4.88	48	=0.01
Concealed nectar	193	5.66	36	
Many stamens	47	4.51	51	<0.005
Few stamens	219	5.66	37	
Polycarpous	24	4.88	39	=0.10
Syncarpous	292	5.54	39	
Hypo- and perigynous	168	5.29	42	<0.60
Epigynous	98	5.46	37	

* Probability that difference between means is due to chance.

Chromatographic analyses of the nectars of forty-four of the species show that a wide range of different amino-acids is to be found, with all essential amino-acids[13] available from the nectar of one species or another. The nectar of *Dianthus barbatus* (Caryophyllaceae), a "butterfly flower", contains at least twelve different amino-acids, the largest number yet found in a single species. Consequently, at least supplemental nutritional value for the flower-visitors can be attributed to the amino-acids of the nectar. Their presence and the apparent selection for their increasing concentration in nectar raise many interesting questions as to the evolutionary mechanisms involved. A detailed report on these continuing studies will be presented elsewhere[14].

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The Pathogenicity of Nodamura Virus for Insects

NODAMURA virus, which was originally isolated from mosquitoes from Nodamura, near Tokyo, multiplies in several insect and tick species, apparently without causing symptoms. It is transmissible to suckling mice by infected *Aedes aegypti*, and is fatal[1]. In Japan young pigs have been found with antibodies to the Nodamura virus, which has been classified as an unusual kind of arbovirus because it is resistant to ether[2]. This property, together with other features of the virus particles[3] are reminiscent of acute bee-paralysis virus[4] and we therefore examined its effect on the honey-bee, *Apis mellifera*. We also tested its pathogenicity for the wax moth, *Galleria mellonella*.

A 2% suspension in 0.01 M phosphate buffer, *p*H 7.0, of homogenized brain tissue from mice killed by Nodamura virus was emulsified with carbon tetrachloride and the supernatant fluid cleared by low speed centrifugation. Adult bees, each injected with 1.0 µl. of the preparation, died after a minimum incubation period of 7 day at 30° or 35° C. Their anterior two pairs of legs became paralysed a few hours before death. The virus was serially passaged in bees, and an extract containing the equivalent of 10^{-7} of a bee killed by Nodamura virus was infective by injection into healthy bees. Isometric particles, about 30 nm in diameter, identical in shape and size to those seen in muscle tissue of mice killed by the virus[3] were purified by triturating infected bees in phosphate buffer with a quarter volume of ethyl ether, emulsifying the mixture with carbon tetrachloride and then subjecting the aqueous phase to cycles of high and low speed centrifugation[5]. Virus preparations reacted strongly in Ouchterlony gel-diffusion tests with antiserum prepared against Nodamura virus and formed single precipitin lines confluent with those formed by the original mouse brain inoculum. Antiserum from rabbits we injected with virus from bees also gave a single homologous precipitin line against virus from bees and mice. Nodamura virus did not react with antiserum to acute bee-paralysis virus. Wax moth larvae injected with an extract containing the equivalent of 10^{-3} of a bee killed by Nodamura virus died, mostly as pupae, after 7–14 day at 30° C. A crude extract of each of these pupae in 1.0 ml. water with 0.2 ml. ether gave an intense single precipitin line, confluent with Nodamura virus from bees, in gel-diffusion tests.

Our results indicate that Nodamura virus is a virulent insect virus of a kind which, contrary to widely held opinions about insect pathogens, can multiply in and kill mammals.

We thank Dr F. A. Murphy for supplying brain tissue of mice killed by Nodamura virus, Professor W. F. Scherer for supplying antiserum, and Dr K. S. Kim for electron microscopy.

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Nature of the Lepidopteron Sensing Mechanism: Possible Photochemical Response

THE complex nature of the moth sensing problem has been demonstrated[1–4]. Here we suggest that the interaction of a moth with its radiation environment may be explained by a chemical change in metabolism induced by the radiation. We have tested this hypothesis by studying the temperature dependence of the behavioural response of several moth species to a black-light source and coherent submillimetre wave radiation.

Behavioural experiments were carried out with equipment previously described[3], in which moths were exposed to uniform radiation in a test chamber. Experimentally, the response of an individual moth was indicated by its attraction to the end of the test chamber at which the radiation source was located.

If the radiation source induced altered chemical metabolism mediated by change of photochemical behaviour, an individual moth would not respond to the radiation stimulus until the chemical reaction had been triggered. Assuming that the moth response follows a first order law, and if C_m is the concentration of moths in the test chamber which have not responded to the radiation, then

$$\frac{dC_m}{dt} = -k\,C_m \qquad (1)$$

where k is the rate constant. That is,

$$\ln(C_m) = -kt + k' \qquad (2)$$

where k' is a constant of integration.

In our experiment with black-light, the source was a 'General Electric F15T8-BL' lamp, having a fluorescent band with a peak in the ultraviolet (below 0.38 µm). The broad fluorescence ended at 0.45 µm and had mercury peaks in it spectrum. Some emission was observed around 8 µm, but this was no greater than a black body at 45° C. There were no significant bands beyond 0.45 µm.

It was found that the response of both the almond moth, *Carda cautella*, and the fall armyworm, *Spodoptera frugiperda*, to the BL source followed first order kinetics. The response of

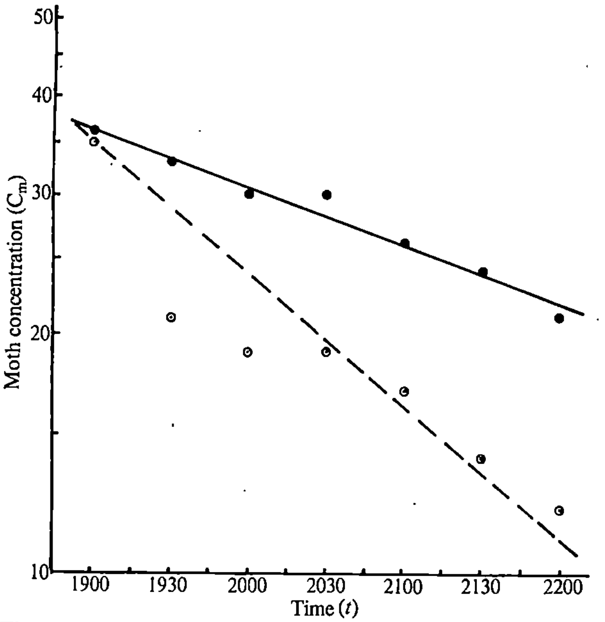

Fig. 1 Response rates of male *S. frugiperda* to a BL source. ●——●, At 20.8°C; ○ – – – ○, at 23.9° C.

male *S. frugiperda* to a 4 W BL source at 20.8 and 23.9° C (Fig. 1) is in agreement with equation (2). We suggest that first order chemical reactions may be involved in the sensing responses.

The rate of response of male and female *S. frugiperda* to a BL source follows the Arrhenius equation (Fig. 2)

$$k = A\,e^{-E/RT} \qquad (3)$$

where A is a constant, T the absolute temperature, R the gas constant and E is the activation energy for the process. A value of 47×10^3 cal mol^{-1} for the activation energy was deduced from Fig. 2. This value is high although not outside the range of normal biochemical reactions.

The same pattern of behaviour was also observed with several other species at different wavelengths with differing rate constants. It appears therefore that this type of response is not uniquely associated with one species of moth or one radiation source. The response of the male corn earworm, *Heliothis zea*, to 311 μm (16 mW) and 128 μm (20 mW) and the male *S. frugiperda* to 311 μm (16 mW) is shown in Fig. 3*a*, as well as the response of male *S. frugiperda* to 7.5 W BL source for comparison. The response rates to coherent submillimetre wave radiation are much higher than that to the BL source, at a fixed temperature the response rate is a function of the radiation wavelength.

The response of male *H. zea* and *S. frugiperda* to 337 μm (50 mW) radiation is shown in Fig. 3*b*, both species show their peak response at this wavelength[3]. The behaviour patterns form two distinct lines with different slopes. The first is triggered rapidly as the radiation source is turned on and ceases after a period of 10 to 15 min; the second has a lower rate constant and persists longer.

This biphasic response pattern could be explained as a 337 μm radiation induced metabolic shift from a rapidly utilized metabolic source to one used more slowly. Based on work by Sacktor and Wormser-Shavit[5] and of other authors[6,7] we believe that the important metabolites involved in this type of biphasic response are glycogen and proline. We suggest that glucose catabolism is greatly stimulated at 337 μm by the release of a neuroendocrine factor such as a catecholamine from the corpus cardiacum[8]. After the first 10 to 12 min of laser exposure, glucose catabolism shuts down and proline catabolized, corresponding to the lower response rate in Fig. 3*b*. The increased rate of glycogen breakdown as shown by accelerated respiratory rates under 337 μm stimulation, is quickly replaced by proline utilization in the Krebs cycle. Unfortunately, the role of proline in the respiration of Lepidoptera has not been fully resolved.

Three factors showing radiation-induced physiological alterations are apparent. First, there is a pronounced stimulation

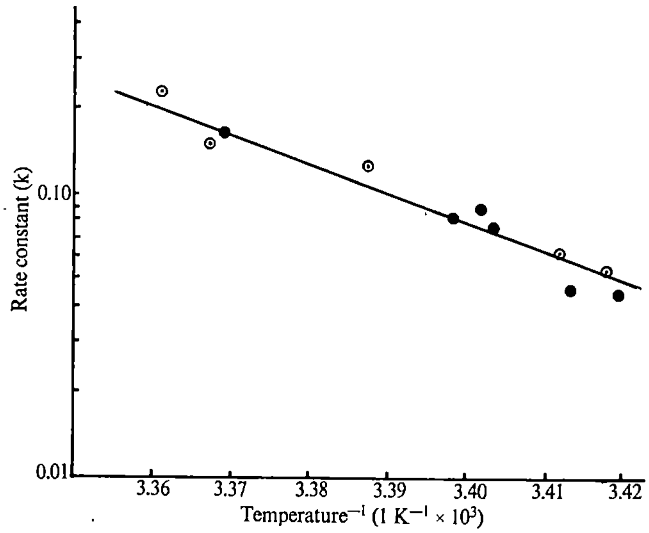

Fig. 2 Response rate constant as a function of temperature. *S. frugiperda* subjected to a BL source. ○, Female; ●, male.

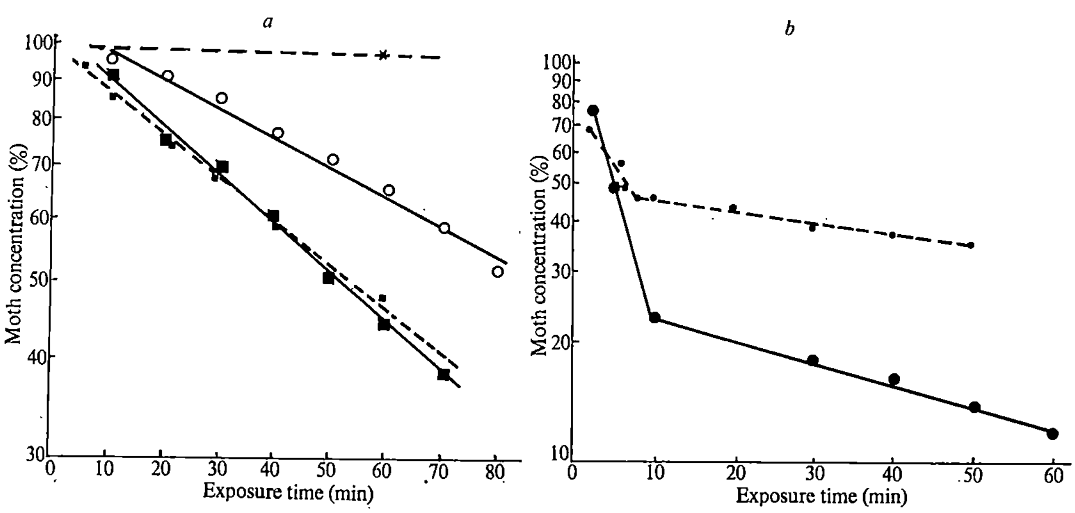

Fig. 3 Response of male *S. frugiperda* (– – –) and male *H. zea* (——) to coherent submillimetre wave radiation. *a*, Radiation wavelengths 311 μm (■); 118 μm (○); BL source (×). *b*, Radiation wavelength 337 μm.

of respiraation by a black-light source. Second, the response to black-light is considerably altered by pre-exposure of moths to 0.6328 μm radiation from a helium-neon laser. Third, irradiating moths with 337 μm radiation inhibits activity and mating potential. We suggest that a chemical process, possibly an enzyme system, is triggered and rate adjusted by radiation exposure.

It is apparent that further studies are needed to increase our understanding of these radiation induced behavioural responses. If stimulation of respiration is triggered photochemically, knowledge of the kinetics involved could result in a method of radiation exposure to stimulate a high percentage of the moth population to the high respiration output. This high output would cause the moths to "burn themselves out" and reduce their life cycle and mating potential, and could be of value as a means of practical control.

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Early Occurrence of Domestic Sheep in Sub-Saharan Africa

Recent excavations by the South African Museum at a coastal cave situated at Die Kelders some 100 miles east of Cape Town have revealed the earliest definite sheep remains in Sub-Saharan Africa.

A minimum of twenty-three individuals were represented and came from a well defined shell midden (layer 2 a/b), two from above and one from immediately below this layer.

A total of nineteen mandibles and maxillae of sheep have been grouped into age categories based on the wear and stage of tooth eruption[1,2]. The results, which are obviously very approximate, indicated the following clustering; four were less than two months old, four considerably older than 40 months (the approximate age at which the last molar erupts), and the remaining 15 were between six to thirty months.

There was good bone preservation because of the alkaline nature of the deposits which underlie the limestone cave roof, and although dentition was counted, other parts were also represented. Sheep and goats are most readily differentiated by the nature of their occipits and horn cores and four of each of these, which definitely belonged to sheep, were represented. Identification was further supported by early reports from the Cape which frequently mentioned sheep but never the presence of goats. These sheep, according to a number of sources[3] (the earliest being Vasco da Gama in 1497), were hairy, non-wool bearing, relatively large and characterized by their broad, fat tails.

A number of radio carbon dates, all from charcoal fragments, have been obtained from this layer. These are GX 1685, 1465±100 years BP=AD 485[4], GaK 3877, 1650±90 years BP= AD300, GaK 3878, 2620±90 years=670 BC, GaK 3955, 1600±120 years=AD 350. There is a date of GaK 3956, 1590±80 years BP=AD 360 for the midden (3) immediately below (2 a/b).

The inconsistency of the 670 BC date may be because samples GaK 3877 and GaK 3878 were not collected *in situ*; in GaK 3878 had been obtained from layer (2 a/b) in a square not fully covered by this layer. The older date is at present considered unreliable.

Comparison of the fauna in the sheep-containing midden with that of the two underlying shell middens which lacked sheep, showed no significant differences either in the relative frequencies or in the condition of the bones. The sheep mandibles, with the exception of a few very young individuals, are characterized by having damaged inferior margins, a feature not observed in the case of small antelope mandibles. Small antelope teeth show no age clustering and individuals of all ages ranging from new-born to extreme old age were present.

Differences in the cultural material were more marked. Layer (2 a/b) had forty-two bone implements, whereas the lower two middens combined had thirty with a 30% greater bulk of excavated material. Midden (2 a/b) contained both decorated incised bone points, a bone "spoon" as well as utilized sheep and bovid scapulae, none of which were found in the underlying middens. In addition it contained eleven bone spatulas known from historical sources to have been used to dehair skin[5] as opposed to only one in midden (4) and none in midden (3). The pottery of (2 a/b) differs in that it includes a decorated pot as well as a spout shard quite unlike the potsherds of other middens. Other finds unique to (2a/b) included perforated *Phalium zeylonica* shells and an unusual piece of mastic which apparently belonged to a four-pronged arrow.

The absence of any locally occurring indigenous sheep, coupled with the known presence of domestic sheep in East Africa *circa* 850 BC[6] suggested that the Die Kelders sheep were a domesticated variety. Differences in cultural material with more sophisticated decorations and greater use of bone suggests, at least, a contact with people other than those responsible for the deposition of the lower middens.

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Radiosensitivity of the Liverwort *Marchantia polymorpha* L. to Internal Radioisotopes

There are very few reports concerned with the effects of internal radioisotopes on the growth of plants. The growth of lateral roots of *Zea mays* is stopped with the addition of 10 μCi ml.$^{-1}$ of ^{3}H-thymidine[1], whereas generally the growth of plants as a whole is not disturbed by doses of radioisotopes normally used for biochemical studies, even though injury, or even growth stimulation may occur in some cases[2].

We present here evidence of very great sensitivity of young plants of *Marchantia polymorpha* to internal radioisotopes ^{32}P

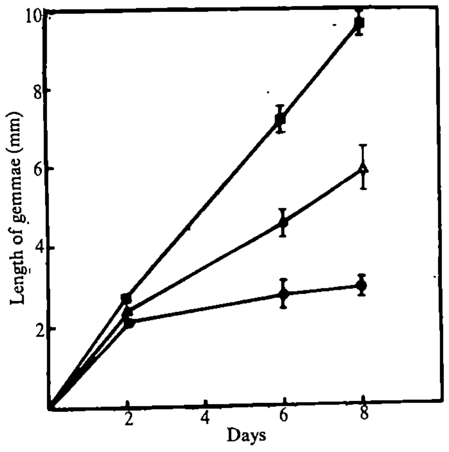

Fig. 1 Effect of internal ^{32}P on the growth of *Marchantia polymorpha*. ■, Control; △, 5 µCi ml.$^{-1}$; ●, 10 µCi ml.$^{-1}$.

and ^{35}S, at doses generally used for labelling. Twenty to twenty-five gemmae from gemmae cups of female *Marchantia polymorpha* were cultivated in Petri dishes on 15 ml. of nutrient solution solidified with agar as indicated by Schneider *et al.*[3]. The growth conditions were continuous illumination at 1,500 lx and a temperature of 22° C. Carrier-free ^{32}P-H_3PO_4 (CEA, Saclay, France) in 0.01 M HCl solution was added to the nutrient medium, and the same amount of HCl was added to the controls.

At a dose of 5 µCi ml.$^{-1}$ of ^{32}P (specific activity: 0.4 µCi µg^{-1} of P) the growth of thalli was seriously inhibited and at 10 µCi ml.$^{-1}$ it was stopped. The inhibiting effect was measurable after 48 h of growth and the difference between control and treated plants was significant after about 3 days of culture. All thalli treated with the radioisotopes were affected and growth inhibition was visible on both length and surface of the thalli. This experiment was repeated several times and the same response was always observed. At doses that did not completely inhibit growth (3 to 8 µCi ml.$^{-1}$) all portions of thalli were uniformly affected.

When carrier-free ^{35}S was used instead of ^{32}P, inhibition of growth was complete for 80 µCi ml.$^{-1}$ (0.76 µCi µg^{-1} of S). As the energy of β particles emitted by ^{35}S is about the tenth of the energy of β particles emitted by ^{32}P we concluded that comparable inhibiting effects were obtained for equal flux of energy. Therefore the nature of the element is not by itself involved in the observed inhibition.

The effect of acute γ-irradiation on *Marchantia* has been investigated by Miller and Sparrow[4]. Contrary to our results with internal radioisotopes they found that the radiosensitivity of vegetative non apical cells was comparable to that of higher plants having chromosomes of similar size. Apical cells possess bigger chromosomes and are more radiosensitive to γ-irradiation. Since entire thalli are uniformly affected by internal radioisotopes, their action could not be the result of damaging chromosomes in the more sensitive apical cells.

It is certainly worth remembering before further studies that thalli of *Marchantia* are haploid and could therefore be more radiosensitive than diploid plants.

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Geographic Differences in Phytoplankton Sensitivity to PCBs

DIFFERENTIAL sensitivity of marine phytoplankton species to chlorinated hydrocarbons has been demonstrated in pure[1,2] and mixed[3] cultures. In particular, the toxicities of DDT (1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane) and PCBs (polychlorinated biphenyls), both widespread pollutants in the marine environment[4], have been investigated. Evidence does not exist, however, for correlating organochlorine sensitivity with the ecological adaptations of the organisms tested.

Previous reports suggest the existence of physiological races of marine phytoplankton. Guillard and Ryther[5] showed *Thalassiosira pseudonana* from the Sargasso Sea (clone 13–1) to be stenothermal and stenohaline, unlike the continental shelf and estuarine isolates (clones 7–15 and 3H). Intraspecific differences in half-saturation constants (K_s) for nutrient uptake have also been demonstrated; isolates from the low-nutrient waters of the Sargasso Sea had lower K_s values for nitrate[6] and silicon[7] than did coastal clones. Such findings indicate that races of phytoplankton are best adapted to their respective environments. Slobodkin and Sanders[8] have postulated that organisms adapted to stable, "predictable" environments would, in general, be more sensitive to environmental stress than would organisms adapted to "unpredictable" surroundings. Experimental evidence for this hypothesis is lacking. We therefore investigated the toxicity of PCBs to three species of diatoms, comparing clones isolated from the relatively stable Sargasso Sea waters[9] with those from fluctuating estuarine environments.

The diatoms tested were *Thalassiosira pseudonana*, *Fragilaria pinnata*, and *Bellerochia* sp.; Fig. 1 presents the clones studied and their isolation sites. (For exact information on dates and sites of isolation, see Carpenter and Guillard[6].) Cells were grown axenically in f/2 medium[5] prepared from Vineyard Sound seawater (salinity = 33‰) filtered through a precleaned Amberlite XAD-2 resin to remove any chlorinated

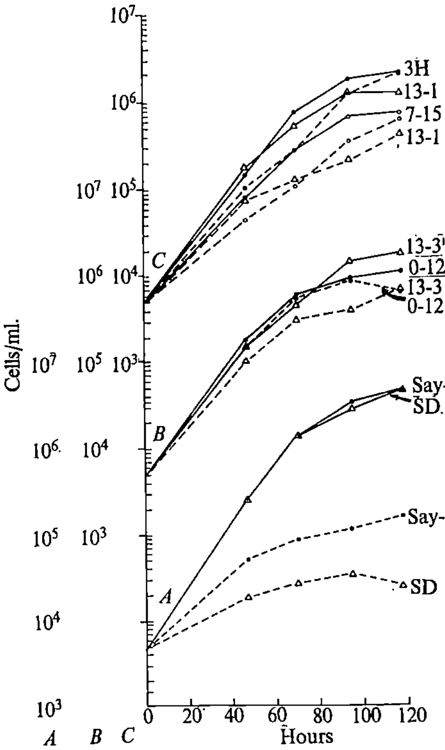

Fig. 1 Growth of (*A*) *Bellerochia* sp., (*B*) *Fragilaria pinnata*, and (*C*) *Thalassiosira pseudonana*. Clones 13–1, 13–3, and SD were isolated from the Sargasso Sea; 7–15 from the edge of the continental shelf; 3H from Moriches Bay, Long Island; 0–12 from Oyster Pond, Massachusetts; and Say-7 from Great South Bay, Long Island. Data points are the means of three replicates. ——, 0 p.p.b.; - - -, 10 p.p.b.

Table 1 Ratios of Mean Cell Densities from Treated : Control Cultures at Five Sample Times

	Hours after inoculation				
	0	47.5	70	95	118
T. pseudonana clones					
3H (estuarine)	1.00	0.694	0.365	0.676	0.976
7–15 (estuarine)	1.00	0.544	0.368	0.520	0.844
13-1 (oceanic)	1.00	0.422	0.241	0.172	0.341
F. pinnata clones					
0–12 (estuarine)	1.00	0.824	0.909	0.932	0.590
13-3 (oceanic)	1.00	0.688	0.707	0.269	0.387
Bellerochia clones					
Say-7 (estuarine)	1.00	0.207	0.064	0.036	0.035
SD (oceanic)	1.00	0.074	0.020	0.013	0.005

hydrocarbon[9a] contamination. Exponentially growing cells were inoculated into sterile, tightly sealed screw cap bottles containing 150 ml. of medium to give an initial cell density of 5,000/ml. The procedure for adding PCBs ('Aroclor 1254') has been described[2]. For each clone, there were three cultures containing 10 parts per 10^9 (p.p.b.) of PCBs and three controls without PCBs. The cultures were maintained at 20° C and illuminated 14 h/day with 5,800 lumens/m^2 from cool-white fluorescent bulbs. Samples of 1 ml. were fixed with 0.05 ml. of Lugol's solution and counted with a Speirs-Levy Eosinophil counter.

Although growth of all seven clones diminished with PCB treatment (Fig. 1 *A–C*), isolates from the Sargasso Sea invariably were more sensitive than were clones from estuaries and the continental shelf (Table 1). Clone 7–15, from the continental shelf, was, in turn, more sensitive than clone 3H, its counterpart from the Moriches Bay estuary. Both *Bellerochia* clones were more sensitive than all others tested, but here, too, oceanic clone SD proved more sensitive than did estuarine clone Say-7. Two-way analyses of variance[10] on the logarithmically transformed data showed that, at 95 h, the interaction term between PCB treatment and geographic origin was significant for *T. pseudonana* ($F(2, 12)=34.56$, $P<0.001$), for *F. pinnata* ($F(1, 8)=31.57$, $P<0.001$), and for *Bellerochia* sp. ($F(1,8)=12.81$, $P<0.01$), indicating algal sensitivity was highly dependent on the sites of isolation.

Natural waters generally contain somewhat lower concentrations of PCBs (one to three orders of magnitude lower) than we employed in our experiments (ref. 11 and unpublished results of G. R. Harvey, W. G. Steinhauer and J. M. Teal), although concentrations exceeding ours have been detected[12]. Concentrations in water may be misleading, however. Organisms are probably exposed to greater amounts of chlorinated hydrocarbons than concentrations in natural waters would indicate because these substances are rapidly removed from water by organisms, including phytoplankton[13]. Holden[14], for example, found no PCBs in Scottish waters but substantial amounts in the resident organisms.

Our results suggest that estuarine-coastal phytoplankton may be better equipped to survive abiotic environmental stress than are those found in the open ocean. These data are therefore consistent with the hypothesis of Slobodkin and Sanders[8].

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Genetic Analysis of Tail Rattling in the Mouse

TAIL rattling is a prominent feature of aggressive encounters between mice and is thought to be a threat behaviour, although conclusive evidence of this is lacking[1]. A factor analysis of aggressive behaviours elicited in a single subject using footshock in conjunction with a bottle brush target indicated that tail rattling had a high loading on the "aggressive factor" and negligible loading on the other factors[2]. On the other hand, a rather comprehensive study of fourteen inbred strains by Southwick and Clark[3] revealed no consistent interstrain relationship between fighting and tail rattling. These displays are usually regarded by ethologists as having complex, rather than unitary, motivational determinants[4]. If this is correct, a linear relationship with a single variable, such as attack behaviour, would be unlikely to prove robust. An additional complication arises when genetic differences between subjects are important. The degree of manifestation or expressivity of the display, in relation to the motivational states which underlie it, may be expected to exhibit genetic variation.

In view of the potential complexity of the processes involved, it is clearly imperative that a simplified experimental paradigm is developed, which allows controlled presentation of relevant stimuli and elimination of uncontrolled behavioural feedbacks. Electric shock has proved quite useful for the study of aggression because it is capable of inducing high rates of aggressive responding between paired subjects[5]. Further simplification is possible in the mouse because many of the behaviours observed in aggressive encounters can be elicited by means of footshock applied to a single subject. I undertook the present study to examine the nature of strain differences in tail rattling elicited by shock, and to assess by means of genetic evidence the relevance of the responses obtained to natural fitness.

Roberts[6] has suggested that the genetic architecture of behavioural traits may be used to assess the relationship of measures obtained in the laboratory to natural fitness, as traits contributing to fitness should display a large amount of nonadditive and little additive genetic variance. A measure of the importance of these components of genetic variance can be obtained by examining a series of crosses between inbred lines. If tail rattling elicited by shock is irrelevant with respect to fitness, the mode of inheritance should be largely additive. If, however, the response to shock is closely related to the disposition to exhibit the trait under natural conditions, and if it is indeed an important social behaviour, then a consistent,

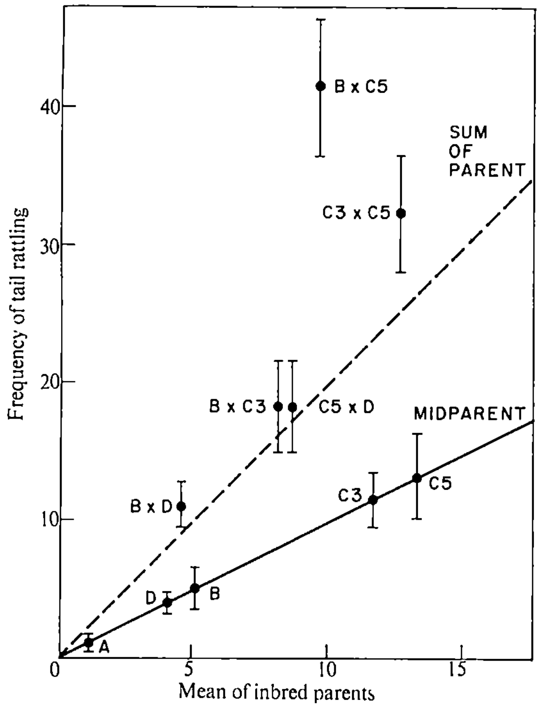

Fig. 1 Frequency of tail rattling of F1 hybrids plotted against the mean of their parent inbred lines. Inbred scores are plotted against themselves and therefore fall on the midparent line (——) defining additive inheritance. All F1's lie above the sum of parent (- - -), indicating that their scores exceed the sum of the mean scores of the parent inbreds (or twice the midparent values).

largely non-additive (that is, heterotic) mode of inheritance should be displayed.

Five strains of inbred mice (DBA/2Ibg, C57BL/6Ibg, C3H/2Ibg, A/Ibg, BALB/cIbg) and five F1 crosses (C57BL × DBA, DBA × BALB, BALB × C57BL, BALB × C3H, C57BL × C3H) were tested. Reciprocal crosses were included for all five, with the exception of the C57BL × DBA cross in which the female parent was C57BL. Experimental subjects were weaned at 25 days, and littermates of like sex were housed together in 27 × 14 × 10 cm stainless steel cages until testing at 60–80 days of age. Approximately ten male and female mice of each strain were tested, with a maximum of two of each sex from any litter.

Subjects were tested in a 16 × 16 × 13 cm 'Plexiglas' box with a grid floor, illuminated to approximately 158 lux by overhead fluorescent lights. The shock source was a 'Stechman' constant current generator and scrambler. The test consisted of four phases; a series of 10 0.2 mA shocks every 20 s, a 120 s recovery period, a series of 10 0.6 mA shocks, and a final 120 s recovery period. The shock duration was 0.5 s throughout.

The response measure we considered was the total number of bouts of tail rattling exhibited over the four phases of the test session. A bout of tail rattling consisted of a series of rapid lateral undulations in the tail. A number of related behavioural changes were typically associated with tail rattling as it occurred both in response to footshock and in aggressive encounters. Pilo-erection was generally observed together with shivering movements of the dorsum skin. When moving, the mouse often displayed the so-called "mincing gait" in which the animal progresses by short steps with the perineal area pulled forward and pressed against the substrate, and in many cases this was accompanied by sporadic urination. Shivering and peculiar urination pattern accompanying the mincing gait was first noted utilizing shock and was subsequently verified by observation of aggressive encounters.

Because of the pronounced heterogeneity of variance between strains, a logarithmic transformation was applied to the original data before analysis of variance and range tests. Analysis of variance of the transformed scores indicated the absence of significant sex and reciprocal differences, and sex and reciprocal groups were therefore pooled. Untransformed scores are reported below for simplicity. All hybrids were significantly higher than the mean of the parent strains, and three were significantly higher ($P < 0.05$, t test) than the high parent. Fig. 1 shows the mean scores based on all four test periods of the F1 hybrids plotted against the mean of their parental strains. The inbred strains were plotted against themselves and therefore lie on the midparent line. If the mode of inheritance were essentially additive, the F1 values would also lie on, or close to, this line. The line defining the values which would be assumed if the F1 scores approximated the sum of the inbred parents' scores is also shown, as it emphasizes the extreme degree of heterosis observed. Of the twenty possible comparisons utilizing the four test periods and five crosses, all exceeded the midparent value and eighteen were higher than the high parent.

Table 1 shows the untransformed mean scores of each inbred strain for each period of the test and the per cent of the total number of responses occurring in each period. The horizontal lines separate strains whose log transformed mean scores for the whole test were significantly different at the 0.05 level using Duncan's multiple range test.

The pattern of responding over the four periods of the test reveals further differences between the inbred strains. BALB, which exhibited 98% of its responses in the first period, can readily be distinguished from DBA, which showed a more even response distribution. Similarly C57BL can be distinguished from C3H on the basis of scores in the second period. A characteristic response pattern can therefore be associated with each of the five inbred lines. While strain differences in behaviour are commonplace, it is rather unusual to be able to discriminate this well among a set of strains on the basis of one class of responses.

It seems quite likely that the present method will prove useful in the investigation of the behavioural organization of this display. It should be extremely useful for genetic analysis of segregating populations, as phenotypes can be assigned to individuals rather than to pairs of combatants. While additional experiments will be necessary for extrapolation from shock induced tail rattling to that which occurs in nature, the heterotic mode of inheritance provides some assurance that the method taps psychological mechanisms related to natural fitness. Finally, the diversity in performance encountered among these genotypes is sufficiently extreme and complex that they may perhaps be used as a model system for the study of the evolutionary development of signal function.

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Table 1 Comparison of Tail Rattling among Inbred Lines

Strain		Period I Low shock	Period II Shock free	Period III High shock	Period IV Shock free	Total score Mean ± s.e.
A	Mean	0.78	0.11	0.17	0.06	1.11 ± 0.35
	(%)	(70)	(9)	(15)	(5)	
DBA	Mean	1.25	0.20	1.90*	0.60	3.95 ± 0.74
	(%)	(31)	(5)	(48)	(15)	
BALB	Mean	4.80	0.05	0.05*	0.00	4.90 ± 1.54
	(%)	(98)	(1)	(1)	(0)	
C3H	Mean	4.76	1.62*	3.95	1.43	11.76 ± 2.2
	(%)	(41)	(14)	(34)	(12)	
C57BL	Mean	3.80	4.65*	3.05	1.70	13.20 = 2.9
	(%)	(29)	(35)	(23)	(13)	

* The BALB strain scored significantly lower ($P < 0.05$) than the DBA strain in period III. The C3H strain scored significantly lower than C57BL in period II.

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Possible Species-Specific
t for Norway Rats

(N-piperidino)-10,11-dihydro-5H-dibenzo (a.d.)-
(Dr J. Morrison, Pfizer Ltd.)) is a compound
ral LD_{50} has been reported to be 6.6 mg kg^{-1}
rats and 1,160 mg in male albino mice[2]. These
that UK 786 might be a highly specific toxicant
e conducted the following series of tests with
of birds and mammals to investigate this.

toxicity tests, single doses of UK 786 were
stomach tube. Propylene glycol solutions
red-winged blackbirds, and the animals
en days post treatment, but for all other
ical was prepared in 0.5% gum tragacanth
on period was 14 days. LD_{50}'s with 95%
ere calculated by the methods of Litchfield
r wild and albino Norway rats and albino
son[4] and Thompson and Weil[5] (for
nd house sparrows). Sprague-Dawley
ebster albino mice, and domestic rabbits
n commercial suppliers, gerbils and bob-
m our laboratory colonies, and all other
rapped. All animals were adults and
ged, except the pigeons, which were

icity tests indicated that of the thirteen
ild and albino Norway rats were highly
ethal action of UK 786 (Table 1).
ng in Norway rats included laboured
is of the extremities, and death usually occurred in 1 to 4 h. Gross pathological examination revealed massive haemorrhaging within the lungs. In other animals that succumbed to UK 786, death occurred two to six days after dosing and no typical symptoms could be identified.

Table 1 Acute Oral Toxicity of UK 786 in Animals

Common name and species	No. and sex tested	Dose (mg kg^{-1})	No. died	LD_{50} and 95% confidence limits
Bobwhite quail (*Colinus virginianus*)	2M, 2F	100	0	
Pigeon (*Columba livia*)	4*	500	0†	
Starling (*Sturnus vulgaris*)	2M, 2F	500	0	
Red-winged blackbird (*Agelaius phoeniceus*)	2M	100	0	
House sparrow (*Passer domesticus*)	6M	—	—	354 (——)
	2F	500	0	
Rabbit, domestic (*Oryctolagus cuniculus*)	3M	500	1	
	2M	100	0	
Deer mouse (*Peromyscus maniculatus*)	4M	1,600	1	
	4F	1,600	1	
Gerbil (*Meriones unguiculatus*)	2M, 2F	500	0	
Rat, ricefield (*Rattus r. mindanensis*)	8F	7.5, 15, 30, 120	0	
Rat, wild Norway (*R. norvegicus*)	12M	—	—	8.4 (5.3–13.4)
	12F	—	—	8.9 (4.4–18.2)
Rat, albino (*R. norvegicus*)	16M	—	—	11.9 (5.7–24.5)
Rat, Polynesian (*R. exulans*)	6M	—	—	354 (——)
Mouse, albino (*Mus musculus*)	40M	—		205 (85.4–492)

* Sex not determined.
† Three of the four birds regurgitated after dosing.

Ricefield, Polynesian, and wild Norway rats were used in voluntary feeding tests with treated bait, made by mixing UK 786 and ground commercial rat chow, and forming the mixture into 105–110 mg tablets. Ricefield and Polynesian rats were each offered one cup containing 10 g of treated tablets for one night. Norway rats were first offered two cups each containing about 20 g of untreated tablets for two consecutive nights; consumption from each cup was recorded daily, and on the third night 20 g of treated tablets were placed in the "preferred" cup and 20 g of untreated tablets in the second cup. Treated tablets were offered for two to four consecutive nights; on subsequent test nights, positions of the treated and untreated cups were alternated.

tion and Mortality when Food Tablets Containing UK 786 were Offered to Individually Caged Rats for One Night

ncentration f UK 786 (%, w/w)	No. and sex tested	Amount eaten				Mortality No.
		Treated food (g)		UK 786 (mg kg^{-1})		
		Mean	Range	Mean	Range	
0.125	4 F	9.9	9.5 –10.0	61.6	52.4– 69.8	0
	5 M	10.0†		56.5	47.3– 69.6	0
0.25	5 F	4.9	1.9 – 7.4	75.2	30.0–122	0
.0	5 F	3.5	2.1 – 6.0	320	189 –468	0
.25	5 F	1.7	1.2 – 2.9	103	55.7–156	0
0	5 F	0.8	0.1 – 2.1	273	12.9–848	0
25	5 F	3.1	0.41– 8.5	36.9	4.6–118	1
	5 M	1.9	0.64– 4.1	21.3	6.8– 45.3	0
	5 F	2.1	0.67– 3.9	45.1	18.2– 90.0	3
	5 M	2.1	0.33– 3.3	46.8	5.7– 81.8	2
	5 F	0.8	0.20– 1.4	50.7	12.1– 97.1	2
	10 F	0.7	0.14– 1.0	56.2	18.3–121	9
	10 M	0.6	0.03– 1.9	34.5	1.5–112	7

rats were offered 10 g of treated tablets only.
it.
20 g each of treated and untreated tablets.

The results of the feeding tests are summarized in Table 2. There was no mortality in ricefield and Polynesian rats offered bait for one night, but acceptance was poor at the higher concentrations. Although Norway rats were offered treated tablets for two to four nights, mortality occurred only the first night; acceptance was also poor at the higher concentrations, but they ate enough 2% bait to cause 80% mortality. After the first night, consumption of treated tablets was highly variable; some animals completely rejected the bait, others ate less than, as much as, or more than the first night.

Public health and agricultural workers have been searching for many years for chemicals for use in Norway rat control programmes that are relatively nontoxic to man, domestic animals and nontarget wildlife. 'Warfarin' has been in the forefront as a rat toxicant, but after the detection of 'Warfarin'-resistant Norway rats in Great Britain[6], and recently in the United States[7], the search for new chemicals to replace it has become more important. Norbormide is selectively toxic to rats[8] but causes "bait shyness". Our primary target species are ricefield and Polynesian rats, but the preliminary data reported here indicate that UK 786 may be a useful rodenticide for Norway rats.

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Migration of Birds over the South Coast of China recorded by Radar

THE opportunity to record bird movements with radar has undoubtedly existed in the Far East, but we know of no published studies of bird migration that utilized radar in Indonesia, Malaysia, Thailand, Vietnam, the Philippine Islands, Taiwan, American Micronesia or even Japan. We report here a radar study of bird migration over Hong Kong (which lies between 22° 9′ and 22° 37′ N and 113° 52′ and 114° 30′ E) to stimulate the use of radar to study bird migrations across or between some of the countries mentioned, and also additional studies on the mainland of China.

During April and May 1972, and again from September to December 1972, we used the 10 cm 650 kW Plessey 43S weather radar of the Royal Observatory, Hong Kong, to detect and study the northward spring and southward autumn migrations of birds over the south coast of China, and particularly over areas immediately to the west, south and east of Hong Kong.

Although there were some breaks in the record, observations were made for nearly four months during 1972.

The findings of detailed ornithologica
mm time-lapse films will be published
some of the results from the period of
are mentioned here to indicate the intere
studies to other sites in the region.

North-eastward movements of birds
mid-April to the end of May in the vici
(and corresponding south-westward
recorded in September and October). W
and partly offshore along the coast, the
echoes involved in this spring movemen
tainly crossing the South China coast
flight from at least as far away as the
Hainan (250 miles) and perhaps from as fa
The character and behaviour of the ec
this movement was mainly of charadriifo
more than 20 species of shorebirds (wad
in Hong Kong during the period from
1972—the three most abundant species
Tringa totanus, Eastern Little Stint, *Cali*
Greater Sand Plover, *Charadrius leschen*

A most prominent ascent of bird echoes
sunset on at least seven evenings in A
Lema Channel and the Pearl River estua
which is uncertain—but perhaps due to te

During the period April 24–28, 1972, ech
apparently arriving at the south coast of
the South China Sea, on at least four afte
that ranged from NNW to NNE with a
NNW–N. Using the RHI facility of the 4
able to determine that these arriving migra
altitudes up to a ceiling of 11,000 foot (ab
three evenings in this same period we
onward departure inland in the same no
both from part of Hong Kong and also fr
islands a little to the south of Hong Kon
of the echoes was of the "passerine-type"
evening departure after sunset. Togethe
of an arrival from the south and a clos
movement northwards in the same di
crossing of the South China Sea of bet
miles to the mainland of China fro
southern Philippine Islands (perhaps
from the north coast of the island of Bo
flight for 36–48 h, by an unidentified
that may have over-wintered even furt

It is thus clear from our preliminary a
that radar studies of bird migration i
countries (which together compose a
"barrier archipelagos" and "inland s
revealing. Furthermore, films made
would dramatically highlight the urgen
inter-governmental measures to conse
fauna that, by virtue of its migrations,
several countries of the region f
Indonesia and Malaysia on the one
and the USSR on the other.

We thank Mr G. J. Bell, director
vatory, for his enthusiastic interest
April 1972 whether bird migration
by this equipment, and subsequen
for recording the migratory move
lapse photography of the radar p

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BOOK REVIEWS

Psychology with a Heart

Psychology is About People. By H. J. Eysenck. Pp. xvii+331. (Allen Lane: London, June 1972.) £3.50.

SOMETHING is stirring in the psychological world: there is a spate of books, broadcasts, and papers which do not deal with technical and detailed issues. Rather they discuss broad questions of principle, perhaps like Professor Hudson in a broadcast attacking "the tyranny of fact" in academic psychology since the war; or perhaps like B. F. Skinner writing a controversial book to argue that an objective and experimental approach is the only way to design a viable culture. Professor Eysenck's book is another contribution of this kind, nearer to Skinner than to Hudson in his views, but nevertheless sharing with Hudson an immediately intelligible and attractive style.

The general thesis of the book is that a hard headed experimental approach is the right one in psychology, but that it is a fallacy to expect the same treatment to produce the same results on all human beings. Rather, Professor Eysenck makes (as he always has done) personality his central variable. The method of argument is to take a number of specific fields: starting with the familiar criticism of psychotherapy as unsupported by objective evidence, moving through Kinsey-like enquiries about sexual behaviour as a function of personality, and leading to a brief popular statement of the claims of behaviour therapy and teaching machines. There is then an argument for the use of intelligence tests and of taking genetic factors into account in education, and a rather wicked discussion of political attitudes as a function of class. Next comes a discussion of pornography and permissiveness in the mass media and finally a lengthy plea for the objective approach on moral grounds.

The strength and weakness of the book can be best illustrated from the section on pornography, which is perhaps the most novel to those who know Professor Eysenck's earlier views. He draws attention to the widespread use by modern therapists of "desensitization" techniques in which a formerly frightening experience is gradually made acceptable by repeated exposure at a safe distance and in a harmless form. This method will sometimes cure irrational phobias: but, he argues, is it not analogous to the repeated presentation of scenes of violence in the comfort of a living room? Might we not explain in this way why "people ask wonderingly why there has been such a terrible outbreak of violence in the USA"?

This kind of point certainly needs discussion. To argue that human behaviour stems entirely from within and is unaffected by cultural experiences would be to deny almost every finding of social psychology. In any consistent culture there ought therefore to be, and in fact are, limits upon the things that can be said or shown without massive disapproval: our society does not in fact tolerate overt racist statements, nor (if they are too blatant) attempts to whip up hatred against particular religions, contempt for women, and so on. What appears on the mass media ought therefore to be considered, to see whether it is going to produce good changes in society or bad ones: for example, whether it might reduce freedom to express divergent points of view.

But Professor Eysenck's argument passes hastily over difficulties. Desensitization frequently fails in the clinic: and we don't really know why. Is it not therefore even more likely to fail in the broader range of experiences met in the living room? Again, even if we admit the applicability of desensitization, we have the problem of identifying the stimuli most likely to produce it. Is a contemporary film with an X certificate really more desensitizing than a traditional cowboy in which blows produce no blood, bullets no mess of skull and brains, and everybody dies decorously and with dignity? Bluntly, has the United States suffered an increase of violence?

These doubts are general throughout the book: things which are true and badly need saying are mixed with things which are uncertain and might be true or false: and occasionally with statements which most other psychologists would regard as very unlikely. No note of increasing doubt appears as one goes from one to another. Perhaps this is inevitable in a book for broad audiences, but it is bound to worry specialists and to make the book slightly dangerous to the general reader. For the latter it ought to appeal by being easy to read: although for the more strait-laced, its impact may be marred by Professor Eysenck's inability to resist a joke. Was it really necessary, for an example of the difficulties of experiment, to describe the procedures for establishing the potency of Prince Vincenzo Gonzaga? Yet there are some instances where Professor Eysenck's taste is impeccable: for example, his choice of the career of a great black scientist, Moses Carver, as a counter-example to those who feel that environment determines educational attainment, and his account of the suicide of a homosexual denied behaviour therapy, as a rebuke to those who regard such therapy as unethical. Passages of this kind convince one that Professor Eysenck's heart is in the right place, and this may do more than any of his technical arguments to win supporters for an approach to human beings based on evidence rather than emotion.

DONALD E. BROADBENT

Fisher's Papers

Collected Papers of R. A. Fisher. Edited by J. H. Bennett. Volume I. 1912–24. Pp. 604. (The University of Adelaide: Adelaide, 1971.) A$17; US$20.

WHAT is achieved by republication of the complete writings of a distinguished scientist? Not, surely, any immediate addition to his science, for what is clearly important in his work will long since have been assimilated to the general body of knowledge. Yet the opportunity of re-reading the original papers instead of subsequent paraphrases by others, of seeing perhaps for the first time work no longer readily accessible, and of tracing the development of major lines of thought can be rewarding and may influence substantially a new generation.

When the author is one who both created, almost single-handed, one field of science and gave much to another, the importance of such publication is incalculable. Ten years after R. A. Fisher died, the University of Adelaide begins a five-volume collection of all his main publications and a few short reviews. These are reproduced photographically from the originals, enlarged or reduced to a standard page size, thus preserving their individuality and an appearance familiar to many. Where available, additional notes and comments by Fisher are added; the editor, Professor

J. H. Bennett, has also incorporated many numerical and typographical corrections as footnotes.

The first volume contains forty-one papers published before 1925. Although during this period statistical theory predominated, Fisher had already manifested a lifelong concern for eugenics and this had stimulated him to make major advances in genetics. The earliest paper, that of 1912 in which he already stated the idea of estimation by maximum likelihood, is an appropriate pointer to a life spent in seeking the optimal use of information. Twenty years later he could assert confidently that "When a biologist believes there is information in an observation, it is up to the statistician to get it out". This volume, of course, includes the great *Philosophical Transactions* paper and others that so firmly established the theory of statistical inference. Here also the study of exact sampling distributions is taken as far as the various beta and gamma types deriving from the normal distribution. Already Fisher had clarified the analysis of contingency tables through specification of degrees of freedom, and had achieved the simplifications in regression theory basic to so much statistical practice today; the papers are now little known but well deserve attention. Yet again, this period includes the beginnings of the analysis of variance. From the need to interpret the classical Rothamsted experiments, Fisher first devised logical instruments for extracting and organizing the information, then saw how this led to new concepts of experimental design; this series of papers still deserves to be read as a counterbalance to the abstract approach so common today.

Though this giant among statisticians was but one among many great figures in genetics, his contribution to genetics was distinctive, important, and influential. Among these early papers appear some of his first steps to reconcile Darwinism and Mendelism; later he was to do much to show the complementarity of the two. Already he showed his interest both in frequencies at and recombinations between major gene loci and in the biometric genetics of characters dependent upon summed effects of many factors. The mastery with which this young man of 28, a mathematician untrained in biology, could write "On the Correlation Between Relatives" was a foretaste of the mark he was to make on quantitative genetics; republication of this frequently quoted paper is particularly welcome. The more specifically eugenic papers may now have little scientific value but they throw light on the man; they illustrate the power with which he wrote, his attention both to detail and to grand design, and his care for the choice of precise word and telling phrase.

This volume is attractive in appearance, pleasant to handle and read, and a credit to both editor and publisher.

D. J. FINNEY

Disks of *Drosophila*

The Biology of Imaginal Disks. Edited by H. Ursprung and R. Nothiger. Pp. xvii+172. (Springer: Berlin and New York, 1972.) 46 DM; $14.60.

PROFESSOR HADORN'S 70th birthday was preceded by a great deal of surreptitious arrangements with publishers. One of the results is a celebratory volume *The Biology of Imaginal Disks.* It is, therefore, a good moment to consider the status of research in this field, and what general problems it can hope to illuminate in the future.

Up to now, studies on disks have passed through three major periods. In the first era, transplantation, dissociation and reaggregation techniques were used to construct fate maps and to investigate the determined state of different regions of the disks. In the second period the maintenance of the determined state was studied. Here two main discoveries were made, one being the great stability of cell type stemming from even small parts of disks transferred from insect to insect and undergoing hundreds of cell divisions. The other, that at a frequency much higher than that for a typical mutation rate, the cells transformed into cells of another disk (transdetermination). Some transdeterminations turned out to be more probable than others. The third major area, still under active investigation now, is the use of genetic mosaics to analyse those cell interactions which lead to pattern formation in the disks. This method has established that determination and transdetermination are phenomena that occur simultaneously in a group of adjacent cells, which do not themselves constitute a clone.

Currently there are signs of a new developmental genetics analysing visible mutants and lethals by techniques combining clonal analysis with experimental transplantations. The main advantage here is that somatic crossing over can be triggered by X-irradiation at any stage of development chosen by the investigator.

All these matters are well discussed in the book. In addition Fristrom and Oberlander report the development of suitable *in vitro* methods and isolation procedures to do biochemistry on disks. It may be too much to hope for some elucidation of the biochemical basis of determination, but there is more cause for optimism with this system than with any other I can think of.

The main appeal of the book is that it is very much alive, squarely set in the present time and conveying the excitement in the field. Even if you do not read it until next year it will be more up to date than most books published in 1973. Imaginal disks are a model system for developmental biologists who should find the book fascinating and challenging. Happy birthday, Professor Hadorn.

P. A. LAWRENCE

Idiosyncratic Astrophysics

Dimensional Analysis and Group Theory in Astrophysics. By Rudolf Kurth. Pp. xiv+235. (Pergamon: Oxford and New York, July 1972.) £7.50.

THIS somewhat idiosyncratic book is interesting but hardly essential reading for workers in the field. In his preface, the author engagingly admits that he had originally envisaged group theory as an underlying theme but that its role in dimensional analysis subsequently appeared less significant. Consequently he has devoted two-thirds of the book to dimensional analysis, with applications to stellar radiation and structure, and the remaining third to reduction of group-invariant systems of differential equations, with application to stellar structure. Examples concerning planets appear in three appendices.

Dimensional analysis is widely used in some branches of physics, but astrophysicists' main use of it seems to be in introductory courses, to give estimates of the order of magnitude of quantities like stellar central temperature. Kurth, however, is trying in this book to make much more serious and extensive use of the technique, and meets with reasonable success. Most of the applications he describes are his own original work. The section on group theory neatly links some well-known methods but contains less that is new.

Kurth's exposition is generally clear and concise, sometimes admirably so, but he occasionally comes irritatingly close to insulting the reader's intelligence. Only once did I find him incomprehensible.

A few specific points should perhaps be recorded. The introductory discussion of the three classical tests of relativity seemed to me top-heavy with assumptions. No reason is given why units of derived quantities are postulated to be monomials of the basic units (which, for example, excludes use of magnitude rather than luminosity). The discussion of the *a priori* probability distribution function for the constants of proportionality is somewhat unsatisfactory, since the criteria for the choice of such a distribution are not examined.

M. A. H. MACCALLUM